American Journal of Diseases of Children

VOLUME 58 SEPTEMBER 1939 NUMBER 3

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OBESITY IN CHILDHOOD

I. PHYSICAL GROWTH AND DEVELOPMENT OF OBESE CHILDREN

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NEW YORK

Obesity is an anomaly of body build characterized by excessive growth in dimension through the accumulation of subcutaneous fat. If this occurs in a fully grown person, the only distinguishing feature will be the increased circumference and the excessive weight. During childhood, however, when growth is a normal process, the problem arises as to how obese children compare with normal ones with regard to those phases of growth which are not expressed by weight.

The growing-up process is complex; it includes dimensional growth and differentiation. The first is commonly measured in a simple way, by the increase in weight and stature. The second can be assessed from the structural progress in skeletal development as visualized in roentgenograms. During later childhood and the preadolescent period the appearance of secondary sexual characteristics is an indication of progressing biologic maturation.

Though the literature on obesity in childhood is extensive, the problem of studying obesity as a variety of growth and development has not been dealt with systematically in previous publications. The reports which refer to the special conditions of obesity during the growth period discuss the subject as it applies to individual observations and as a more or less incidental finding.

Czerny and Keller,[1] citing the older literature and referring to their own observations, drew attention to the fact that obese children fre-

This investigation has been aided by a grant from the Josiah Macy, Jr. Foundation.

Part of the material contained in this paper was presented at a meeting of the Society for Pediatric Research on May 4, 1938 (Am. J. Dis. Child. **56**:940 [Oct.] 1938).

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1. (*a*) Czerny, A., and Keller, A.: Des Kindes Ernährung, Ernährungsstörungen und Ernährungstherapie, ed. 2, Leipzig, Franz Deuticke, 1928, vol. 2, p. 621. (*b*) Keller, A.: Beobachtungen über Adipositas im Kindesalter, Fortschr. d. Med. **45**:7, 1927; (*c*) Weitere Beobachtungen über Adipositas im Kindesalter, ibid. **47**:130, 1929.

quently also excel in height and in other dimensions. They mentioned in particular large bones and joints and were inclined to call the condition gigantism as well as adipositas. According to their statement, the excessive growth of the bones precedes the onset of obesity by several years; children with slender bones do not become obese. The authors considered this as proof that obesity develops on the basis of a constitutional anomaly; Keller [1c] concluded that during the period of growth and during puberty different laws are valid for the children inclined to become fat. Rosenstern [2] reported similar observations for obesity during puberty. In recent German contributions [3] unusually tall obese children are classified as presenting adipositas-gigantism, a subdivision of the endogenous type of obesity. Hanssen,[4] reporting 5 cases from Denmark, discussed the increased height of obese children as a special type of obesity. Ellis and Tallerman,[5] in London, found the majority of 50 patients to be slightly above the average in height for their age and sex; in no case was there a considerable statural retardation. As these measurements were all made about the period of puberty, when the normal variation is considerable, the authors did not wish to postulate a condition of hyperpituitarism to account for their finding.

Nobécourt [6] reported from Paris the statural development of 50 obese boys and 50 girls, whose ages ranged from 6 to 18 years. He found a great variation in height, though that of the majority of his patients fell within a normal range. One third were above the mean in height for their age, while definite retardation was found in only 9 cases; 1 of the undersized children suffered from tumor of the brain (craniopharyngioma); another was a mentally retarded boy with malformation of the head. Serial observations on a smaller group of patients showed a wide variation in the increment in stature over a given time. In this communication no reference was made to the onset of puberty.

Gordon,[7] whose 50 patients ranged in age from 5 to 17 years, found 37 children within the limits of normal height for age; 8 were above the

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2. Rosenstern, J.: Ueber die körperliche Entwicklung in der Pubertät, Ergebn. d. inn. Med. u. Kinderh. **41**:838, 1931.

3. (*a*) Opitz, H.: Adipositas-Gigantismus, Kinderärztl. Praxis **4**:549, 1933. (*b*) Reye, E.: Ueber Adipositas-Gigantismus im Kindesalter, ibid. **6**:149, 1935. (*c*) Priesel, R., and Frey, L.: Fettsucht im Kindesalter, Arch. f. Kinderh., 1938, supp. 15. (*d*) Hering, S.: Die Formen der kindlichen Fettsucht und ihre Prognose, Monatschr. f. Kinderh. **73**:11, 1938.

4. Hanssen, P.: Obesity During Growth, Acta med. Scandinav. **91**:435, 1937.

5. Ellis, R. W. B., and Tallerman, K. H.: Obesity in Childhood, Lancet **2**:615, 1934.

6. Nobécourt, P.: La taille des enfants et des jeunes gens obèses, Gaz. d. hôp. **110**:1565, 1937.

7. Gordon, M. B.: Endocrine Obesity in Children: Clinical and Laboratory Studies and Results of Treatment, J. Pediat. **10**:204, 1937.

average and 5 were below. Dorff,[8] in his studies on maldevelopment of the testes, classified a group of boys who were overgrown and some of whom were obese as exhibiting a special form of adiposogenital dystrophy due to primary hypogonadism.

I am not familiar with a detailed study of skeletal development of obese children. Priesel and Frey [3c] mentioned that skeletal maturation was normal in their cases; in some instances a certain degree of acceleration was noted. Dorff [9] described a certain group of children who were characterized by retarded osseous development as showing "masked hypothyroidism;" of his 40 subjects 28 per cent were overweight to some degree.

Several articles deal with the later development of obese children, emphasizing the prognosis with regard to sexual maturation and onset of puberty. According to all observations, obese girls attain puberty at a normal or even an early age. No significant menstrual difficulties or irregularities were noticed. As for boys, Nobécourt,[10] reporting the sexual development of 100 obese children in a separate article, found no significant deviation in the onset of puberty; most of his boys showed a puberal development conforming with the average; in a few the onset or conclusion of puberty was somewhat precocious or delayed, but not beyond the normal range. He advised that when puberty is abnormal a special study of the case be made; obesity and hypogenitalism may occur together, but they are independent manifestations. Ellis and Tallerman [5] observed in their material that normal onset of puberty was the rule, with the exception of the occasional precocious menarche in girls. Hering [3d] and Bornhardt [11] reported an occasional case of delayed puberty in boys; their patients, however, were only 12½ to 15 years old at the time of the follow-up study. Gordon [7] and Dorff [8] instituted active endocrine treatment, so that no information as to the course of spontaneous development can be obtained from their work.

While the European literature relating to obesity in childhood shows a definite tendency to treat the condition as a constitutional anomaly or as an exaggeration of the pre-adolescent increase in weight, Amer-

8. Dorff, G. B.: Maldevelopment and Maldescent of the Testes: Report of Treatment with the Anterior Pituitary-like Gonadotropic Hormone, from the Urine of Pregnant Women, Am. J. Dis. Child. **50**:649 (Sept.) 1935; II. Further Observations on Treatment with the Anterior Pituitary-like Gonadotropic Hormone, ibid. **50**:1429 (Dec.) 1935.

9. Dorff, G. B.: Masked Hypothyroidism in Children, J. Pediat. **6**:788, 1935.

10. Nobécourt, P.: Obésité et puberté, Presse méd. **46**:4491, 1938.

11. Bornhardt, M.: Ueber Fettsucht im Kindesalter und ihre Prognose mit besonderer Berücksichtigung der Frage der Dystrophia adiposogenitalis, Monatschr. f. Kinderh. **67**:270, 1936.

ican authors, in original contributions as well as in textbooks[12] and reviews,[13] have emphasized the significance of endocrine dysfunction and given elaborate outlines for classification of obesity. In the definition of the different types, retarded statural growth, delay in the appearance of the ossification centers, undeveloped genitalia and infantilism are cited as essential for the diagnosis of obesity of endocrine origin. The reports, however, do not convince one that all these features are regularly or even commonly encountered in the obesity of childhood, although an occasional case report may deal with a retarded child[14] in whom adiposity was found in addition to other developmental abnormalities.

In view of these discrepancies, it seems desirable to study the growth and development of a large group of children whose obesity was the outstanding clinical symptom. Since puberty is associated with and followed by an acute change in the growth pattern, it is important to consider separately patients of different ages; only children in whom obesity developed before puberty are included in this study. No attempt was made to classify the cases according to endocrine terminology. One aim of the study was to establish an objective basis for the diagnosis of the underlying endocrine disorder, if any, through an analysis of the progress in growth. It was hoped that an evaluation of the data in comparison with recent results of studies on longitudinal growth would help to clarify the peculiarities of growth and development in obese children.

MATERIAL

The present communication is based on observations of 102 obese children ranging in age from 2 to 13 years who were studied during the last two and a half years in the Pediatric Division of the Vanderbilt Clinic and at the Babies Hospital. This figure includes all obese children who came to my attention during that period, with the exception of those in whom primary mental deficiency was the outstanding disturbance and who presented a qualitatively different problem. I did not exclude children suffering from tumor of the pituitary gland, the midbrain or the adrenal cortex. On the contrary, each child was scrutinized carefully for these possibilities; in no case did the customary clinical and laboratory examinations reveal anatomic changes which might be the cause of the obesity.

The group comprised 51 boys and 51 girls. The equality of the figures is accidental and indicates that the number of obese children who present themselves for treatment is approximately the same for both sexes. The degree to which these

12. Holt, L. E.: Diseases of Infancy and Childhood, ed. 10, edited by L. E. Holt Jr. and R. McIntosh, New York, D. Appleton-Century Company, 1936, p. 609. Griffith, J. B. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, 1937, p. 1089.

13. Hess, J. H., and Kunstadter, R. H.: Diagnosis and Treatment of Obesity in Children, M. Clin. North America **22**:161, 1938.

14. Pinckney, M. M., and Main, R. J.: A Case of Infantile Adiposis Treated with Thyroid, J. A. M. A. **107**:1966 (Dec. 12) 1936.

children deviated from the normal weight is noted as percentage of overweight in comparison with the standards of Baldwin and Wood,[15] which take height and chronologic age into consideration. The average percentage of overweight in my group was 44.8 for boys and 46.3 for girls. Figure 1 demonstrates the distribution of the excessive weight. There were no significant differences between boys and girls. An excess of 40 per cent may be chosen as the border between moderate and severe obesity. In both groups about half of the subjects were between 20 and 40 per cent overweight; the rest suffered from a severe degree of obesity. An excess of more than 100 per cent was found in 1 boy and in 2 girls.

All children who came under observation were American born; the majority of the parents either were of foreign birth or had partly retained the culture of

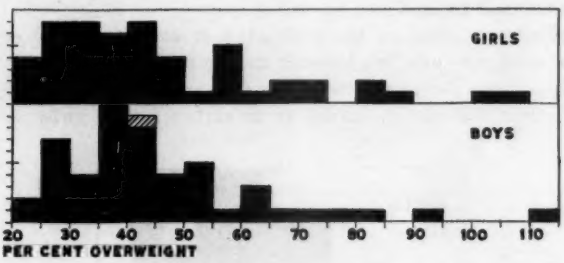

Fig. 1.—Degree of obesity expressed in percentage of overweight. The number of cases is represented on the vertical axis.

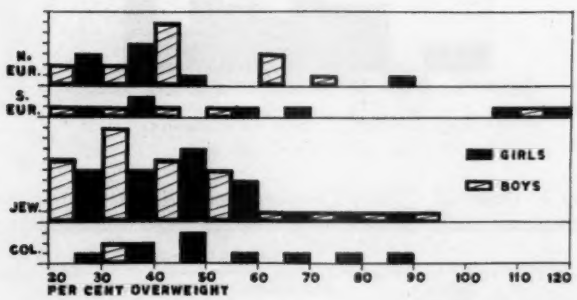

Fig. 2.—Nationality and degree of obesity. "N. EUR." indicates North European stock; "S. EUR.," South European stock; "JEW.," Jewish descent, and "COL.," Negro American stock.

the country of origin. Among the boys, 30 were of Jewish descent, the majority of the parents coming from Eastern Europe; 8 were white American, 3 Scotch-Irish and 3 Italian; 1 each was of Russian, Greek, Spanish, Dutch or German-Swedish stock; 2 boys were Negroes. The distribution among the girls was similar; the only significant difference was in the group of Negroes, of whom 10 were girls. The other nationalities were represented as follows: Twenty-

15. Baldwin, B. T., and Wood, T. D.: Weight-Height-Age Tables, New York, American Child Health Association, 1920.

five girls were Jewish, 4 white American, 3 Italian, 2 each of Scotch-Irish, Hungarian, Greek or German descent and 1 of Dutch origin. No difference in the ages at which the children of different nationalities presented themselves for treatment is noted in my figures. The relation between different national origins and severity of obesity is illustrated in figure 2. The most severe forms were met with in children of South European stock, while the children of North European stock generally came for treatment at an earlier stage. One gains the impression that among the large group of Jewish children the boys who sought treatment had less severe degrees of obesity than the girls. It is doubtful whether the distribution of this group of clinic patients corresponds to the actual incidence of obesity in the child population of different nationalities. It appears that the indifference or sensitivity toward pathologic conditions varies a good deal for the different national groups.

The distribution of age at the time of first examination is represented in figure 3. The peak for girls lies between the ages of 8 and 10 years; the largest number of boys came for treatment between 10 and 13 years. One might deduce from these figures that obesity occurs at an earlier age in girls. A comparison,

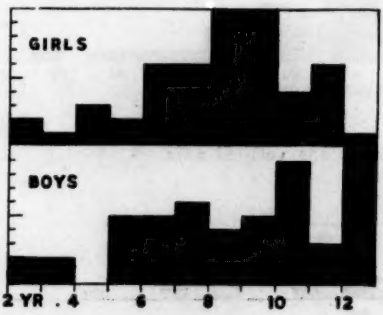

Fig. 3.—Age at first examination.

TABLE 1.—*Age at Onset of Obesity Compared with Age at First Examination**

	Onset of Obesity							
	Infancy, 0-1 Yr.		Childhood, 1-8 Yr.		Preadolescence (After 8 Yr.)		Not Recorded	
Age at Examination	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
2 - 4 years	2	2	1	1	..	..	1	..
4 - 6 years	2	1	2	2	..	..	1	2
6 - 8 years	3	6	6	5	..	..	2	1
8 -10 years	2	1	6	9	1	1	..	9
10 -12 years	3	1	2	5	6	3	1	1
More than 12 years	2	1	3	..	4	..	1	..
	14	12	20	22	11	4	6	13

* Three boys and 2 girls who had been obese since infancy showed rapid gain in weight during the period of preadolescence and came at that time for treatment. They are included in the group who had onset of obesity during infancy.

however, between the age at the onset of obesity and the age at first examination (table 1) fails to confirm this; no significant difference exists between the ages at which obesity develops in the two sexes. The apparent difference between

the ages at first examination must find its explanation in factors outside the actual somatic condition; it points to social and psychologic circumstances which cause girls to become concerned about their size at an earlier age than boys.

WEIGHT AT BIRTH AND EARLY DEVELOPMENT

Information regarding the weight at birth was obtained for 45 boys and 45 girls. The few cases in which no figure but the description "normal" or "rather heavy" was given are added to the columns of 7 to 7½ pounds (3,175 to 3,402 Gm.) and 8 to 8½ pounds (3,629 to 3,856 Gm.), respectively, in figure 4. With the exception of 2 boys whose weight at birth was given as more than 11 pounds (4,990 Gm.), the variation of the weights is not significantly different from that of newborn infants who did not become obese during childhood. In my material no correlation could be found between the weight at birth and the later development or the clinical course of obesity. The

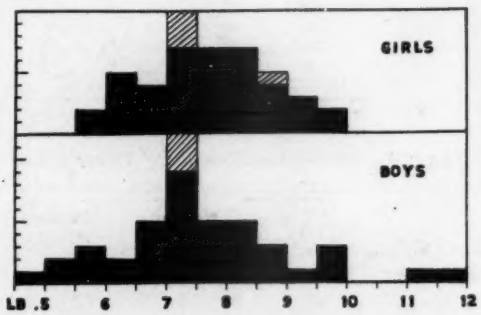

Fig. 4.—Weight at birth.

TABLE 2.—*Weight at Birth and Age at Onset of Obesity*

Weight at Birth	Onset of Obesity: Infancy, 0-1 Yr.		Childhood, 1-8 Yr.		Preadolescence (After 8 Yr.)		Not Recorded	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Not recorded.....	2	..	3	3	1	..	1	2
Less than 6 lb.....	..	1	4	1	2	..	..	..
6-8 lb.....	7	4	8	11	6	3	3	9
More than 8 lb.....	5	7	5	6	2	2	2	2

relation between weight at birth and age at onset of obesity is brought out in table 2. Excessive weight at birth does not necessarily lead to early onset of obesity, and a normal or even low weight is frequently encountered in children who grew fat at an early age. In the search for a constitutional factor in the development of obesity, the high weight

at birth is frequently cited as an expression of a specific predisposition. But a high weight at birth was found only in rare instances in my series. Furthermore, children whose weight at birth was unusually high have been found by Orel [16] to become obese in only a small number of cases. No information could be obtained regarding the length at birth.

Delay in dentition and in locomotor and mental development are well known features of hypothyroidism. Information about the onset of these functions was obtained for more than 40 obese children, though in each case not all three data were remembered. Although the information supplied by parents is not invariably correct and their interpretations as to onset of walking and talking vary a good deal, they

TABLE 3.—*Early Development of Obese Boys*

Age	Walking	Talking	Teething
Before 6 months	..	..	12
6-12 months	7	11	22
12-18 months	33	24	2
18-24 months	4	6	..
After 2 years	1	3	..

TABLE 4.—*Early Development of Obese Girls*

Age	Walking	Talking	Teething
Before 6 months	..	..	8
6-12 months	10	4	31
12-18 months	31	33	2
18-24 months	2	3	..
After 2 years	2	1	..

generally remember with greater exactness any early or late development. The data, presented in tables 3 and 4, show that normal development was the rule. Dentition sometimes occurred early but in no case before the fourth month. The few children who commenced walking or talking after the second birthday did not show a simultaneous delay in both functions or signs of physical or mental retardation later. No difference in early development could be found between the children who gained excessive weight during infancy and those whose gain commenced later in childhood.

GROWTH IN STATURE

The pertinent data are presented in tables 5 and 6, arranged according to the age at first examination. In a few instances, when figures more than one year apart were available, they are given also. A few more

16. Orel, H.: Ueber Riesenwuchs der Neugeborenen und deren späteres Schicksal, Ztschr. f. Konstitutionslehre **16**:435, 1932.

TABLE 5.—*Data on Obese Boys*

Case No.	Patient	Age Yr.	Age Mo.	Height, In.	Weight, Lb.	Percentage Overweight	Height Age, Mo.	Skeletal Age, Yr.	Sexual Maturation
1	H. D.	2	4	38¼	55	67	38	2½	Normal
2	Sh. G.	2	6	37½	40	25	35	..	Undescended testicle†
3	L. R.	3	6	42¼	57	46	57	..	Normal
		7	7	51	81	33	108	..	
4	Ch. C.	3	9	40	51	42	46	3½	Incomplete descensus
5	F. B.	5	3	44¾	69	53	70	..	Normal
6	T. A.	5	4	45½	63	34	76	6	Normal
7	P. R.	5	7	46½	77	57	80	6-7	Normal
		7	7	51½	90	45	109	8+	
8	J. Sch.	5	8	47¾	77	54	88	7+	Incomplete descensus†
9	H. B.	5	10	48¾	74½	54	82	6-7	Normal
10	M. N.	6	3	48¾	70	30	94	7+	Normal
11	N. Z.	6	6	49½	87	37	98	8-9	Incomplete descensus
12	W. G.	6	7	53¼	82	24	122	8	Incomplete descensus
13	J. O'C.	6	7	50¼	91	60	104	..	Normal
14	R. Y.	6	7	50	85	32	102	..	Normal
15	H. M.	7	1	52½	97	42	117	..	Normal
		9	1	57	128	62	148	..	
16	S. G.	7	4	54¼	97	39	128	..	Incomplete descensus
17	W. O'G.	7	4	50	93	63	102	8	Normal
18	A. H.	7	6	49¾	71	25	100	..	Normal
19	H. G.	7	7	48¼	80	51	90	7½	Normal
20	G. B.	7	7	53¾	95	36	126	..	Normal
21	S. G.	8	..	53¾	106	52	126	..	Normal
22	A. L.	8	1	54	102	46	128	..	Normal
23	E. J.	8	4	"Tall"	111	About 40	Advanced	10½	Normal
24	S. S.	8	11	51½	86	39	111	..	Normal
		11	1	55¾	99	32	142	..	
25	M. S.	9	..	56	103	35	141	8+	Normal
26	B. C.	9	..	56	106	40	141	..	Normal
27	R. P.	9	4	54	88	26	128	..	Normal
28	St. F.	9	8	56½	106	38	144	10	Normal
29	F. B.	9	9	54¼	96	35	130	10	Incomplete descensus†
30	J. N.	10	..	55½	94	29	138	..	Normal
31	G. T.	10	..	54	120	71	128	..	Normal
		11	9	57	149	84	146	13	Puberty at 12 yr.
32	S. L.	10	2	59½	106	29	160	11½	Normal
33	F. K.	10	3	53¾	93	33	126	..	Incomplete descensus†
34	S. A.	10	5	60	132	43	163	11½-12	Normal
35	G. K.	10	6	56½	112	43	144	..	Normal
36	H. L.	10	9	55	122	70	134	11+	Normal (spontaneous development)
37	R. v. A.	10	9	55	106	45	134	11	Normal
38	B. F.	10	10	58	154	83	153	12½	Normal (spontaneous development)
		12	..	61	154	60	168	13¾	
39	N. S.	11	1	65¼	104	37	142	..	Puberty
40	M. M.	11	5	60½	119	28	166	..	Puberty
41	S. T.	11	9	64½	141	27	186	12-13	Normal
42	N. F.	11	10	56½	92	20	144	..	Normal
		13	6	59¾	113	19	164	..	Puberty
43	J. G.	12	..	59½	171	90	160	..	Puberty
44	P. Z.	12	..	59¾	131	42	164	..	Incomplete descensus
45	J. P.	12	1	59	129	43	158	..	Incomplete descensus†
46	H. P.	12	4	55	100	39	134	11¼	Normal
47	S. Sh.	12	5	58¼	115	35	154	..	Incomplete‡
48	S. R.	12	6	57½	121	50	150	..	Puberty
49	D. F.	12	9	62½	159	47	174	13-14	Orchidopexy,‡ puberty at 14 years
50	E. P.	12	10	57	151	115	148	..	Small
51	L. R.	13	1	62¾*	152	43	175	..	Puberty

* Deformity of spine (spondylolisthesis).

† Treated with a gonadotropic substance from the urine of pregnant women (follutein, Squibb).

‡ Treated with a gonadotropic substance from the urine of pregnant women (antuitrin S).

TABLE 6.—*Data on Obese Girls*

Case No.	Patient	Age Yr.	Age Mo.	Height, In.	Weight, Lb.	Percentage Overweight	Height Age, Mo.	Skeletal Age, Yr.	Sexual Maturation
1	A. Y.	2	..	37¼	52	68	36	2	Pseudobreast
2	S. B.	2	8	37¾	49	48	38	3½	Normal
3	M. S.	3	5	39¼	48	41	44	..	Normal
4	B. P.	4	..	41	48	30	52	..	Normal
5	E. R.	4	6	39½	49	40	45	..	Pseudobreast
6	S. S.	4	10	43¾	54	29	68	..	Normal
7	M. E.	5	1	44	55	40	68	6-7	Normal
8	D. K.	5	10	47½	70	37	88	..	Early puberty suspected
		10	6	56	113	45	138	..	Prepuberty; no menstruation
9	J. W.	6	..	48	69	33	92	8+	Pseudobreast
10	F. P.	6	1	49½	81	47	100	7-8	Normal
		7	8	53	94	42	122	10	Pseudobreast
11	J. S.	6	4	45	60	25	74	7	Normal
12	S. R.	6	4	47½	67	31	88	7¼	Pseudobreast
13	B. T.	6	7	48½	82	55	94	7-7½	Normal
14	G. B.	6	10	48¼*	112	115	92	10	Normal
15	G. F.	7	..	49½	84	53	100	..	Normal
		8	..	51½	92	53	114	..	Normal
16	M. B.	7	1	50½	104	83	106	9¼	Pseudobreast
17	A. C.	7	1	51½	94	54	114	10-11	Normal
18	B. L.	7	6	53¾	92	33	127	..	Normal
		10	5	59½	121	36	156	10½	Prepuberty
19	E. B.	7	8	52½	97	49	120	8+	Normal
20	T. S.	7	9	53½	101	55	126	..	Normal
21	H. K.	8	10	51	76	27	110	..	Normal
22	Y. M.	8	4	53¾	110	57	126	..	Pseudobreast
23	C. B.	8	7	51¼	86	43	112	8¾	Pseudobreast
24	A. E.	8	8	51	73	24	110	..	Normal
25	A. C.	8	8	55¼	125	74	134	..	Normal
26	G. G.	8	8	51¼	85	31	112	..	Normal
27	A. S.	8	6	48	72	39	92	8-9	Normal
28	M. B.	8	9	50	76	36	104	9½-10	Normal
29	M. Z.	8	9	50½	103	81	106	9½-10	Pseudobreast
30	C. P.	8	10	53½	93	37	126	..	Normal
31	E. McG.	8	10	56	110	45	138	..	Prepuberty
32	B. G.	9	2	51¾	84	31	115	10	Prepuberty
33	A. McL.	9	5	57	103	29	144	11-12	Prepuberty
34	E. C.	9	6	56¾	141	86	142	..	Normal; menstruation
		11	5	61¼	143	45	168	..	before 12 years
		13	1	64	128	12	>17 years	15	
35	S. G.	9	6	56¼	91	20	142	..	Normal
36	A. B.	9	6	54	99	43	128	..	Normal
37	M. M.	9	9	62½	127	22	192	11-12	Menstruation at 10½ years
38	A. C.	9	10	57	117	43	144	12½	Prepuberty
39	G. P.	9	10	55¾	94	27	138	..	Normal
40	G. M.	9	11	55½	108	44	136	11½	Prepuberty
41	R. W.	10	5	57½	112	35	146	11½	Normal
42	F. R.	10	5	56¾	106	29	142	..	Normal†
		11	9	58¾	124	42	152	10+	Normal
		12	10	61¼	131	31	170	12¾	Prepuberty
43	G. W.	10	7	58½	148	74	150	15-18	Menstruation at 9 yr.
44	L. S.	10	9	62¼	164	56	184	14+	Menstruation before 10 yr.
45	R. K.	11	3	56	112	47	138	11½	Prepuberty
46	M. H.	11	7	58¼	109	30	148	12¼	Pseudobreast
47	J. A.	11	8	61	132	66	166	12-13	Prepuberty
48	J. F.	11	9	58¼	132	60	150	12	Menstruation at 11 yr.
49	H. S.	11	10	57¼	112	38	146	..	Menstruation at 12 yr.
50	L. N.	10	2	54¾	89	20	132	..	Normal; menstruation
		14	..	62	127	22	178	14	at 13 yr.
51	I. V.	13	4	59¾	189	100	158	13½	Menstruation at 13 yr.

* Deformity of lower extremities (dyschondroplasia).
† Left oophorectomy for cystic ovary at age of 8 years.

of these longitudinal data are used in the preparation of the charts. Height age was calculated from the two height charts prepared by Burgess,[17] which were constructed after statistical analysis of sixty studies of growth in stature of American boys and girls; they are best suited for my study, since the group comprised children of mixed racial background. "Height age" in my tables and charts indicates the age in months at which the "average" child of the same sex (Burgess's fiftieth percentile) attains the same height as the child under comparison. The relation of height age to chronologic age is graphically demonstrated in figure 5*A* for the boys included in this study and in figure 5*B* for the girls. The patients' chronologic ages are plotted along the abscissas and the height ages along the ordinates. The straight line rising at 45 degrees from the horizontal represents the line at which the two values

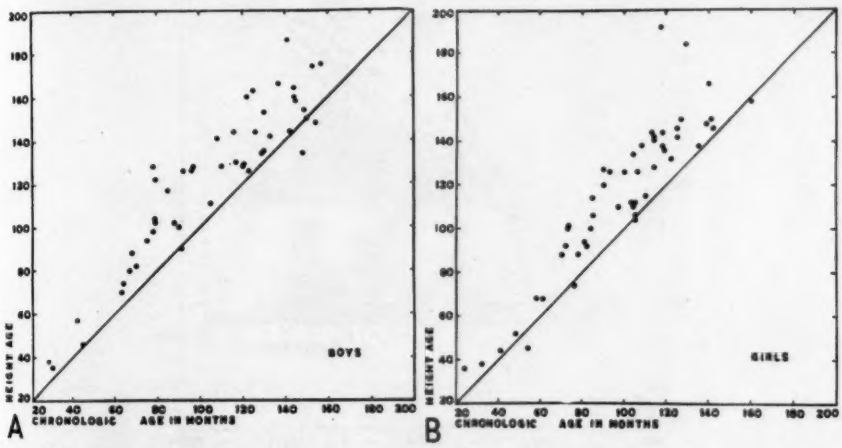

Fig. 5.—*A*, height age compared with chronologic age of obese boys. *B*, height age compared with chronologic age of obese girls.

are equivalent. If one were dealing with an unselected group of children, one would expect that a majority of marks would fall on this line, which represents subjects whose height age and chronologic age are identical; the rest would be distributed evenly above and below this line. The two charts show that the height development of the obese child is different from the mean. With few exceptions the marks are above the line, showing that the obese children of this study tend to be advanced in stature.

Though the acceleration appears to be more marked for the older children, coinciding with the pre-adolescent spurt in growth, it is found

17. Burgess, M. A.: Construction of Two Height Charts, J. Am. Statist. A. **32**:290, 1937.

also for young children. In a number of cases longitudinal data on the same child were obtained, either from clinical records or from other written records preserved by the parents. They are presented in figure 6; marks representing the same child are connected by a line. If the slope of this line is parallel to the 45 degree line, it indicates that the rate of statural increment is the same as that of an average normal child. A larger—(more obtuse)—angle with the horizontal line expresses the fact that this child is growing faster than most other children of his age. The majority of the subjects showed either a normal rate or a slight acceleration of growth. Only a few showed the

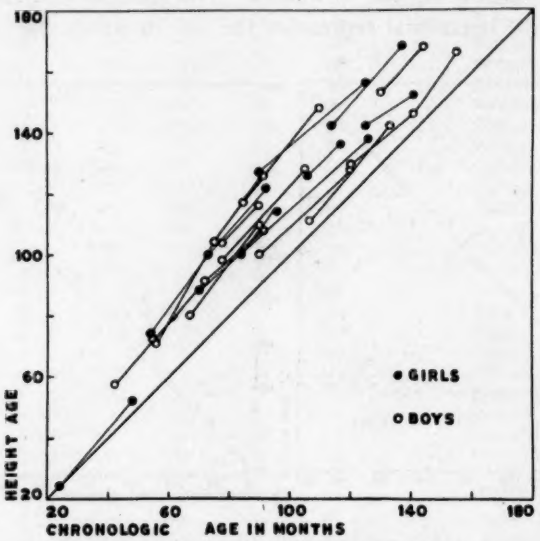

Fig. 6.—Progress in height development of obese children.

opposite behavior, a declining rate of growth. This was found for girls who had undergone early puberty.

The amount of height difference expressed in months of height age is illustrated in figure 7. A normal group would have its peak over the zero line, which would indicate that the attained height was equivalent with the expectancy for the given age. On the left of the zero line are the patients who were behind their age peers in height development; on the right, all those who were advanced. The height age of two thirds of the patients was within two years of the normal age, a deviation which in itself falls inside the normal range. The important point is that the distribution of the whole group shows a definite skewness in the direction of excessive height. About a third of the children were advanced more than two years. These children

were conspicuous by their stature on direct inspection. They probably had the type of condition to which the term adipositas-gigantism has been applied.[18] Their conspicuous stature, however, represents merely a symptom which, to a somewhat lesser degree, is characteristic of the entire group of obese children. The apparent difference between my observations and those of other authors can be attributed mainly to the circumstance that previous reports dealing with patients up to 18 years of age have not given due consideration to the decisive influence of puberty on the growth process.

The increased size of the obese child was brought about by excessive growth in all dimensions. No simple relation, however, existed between the development in height and in weight. Though the two factors moved in the same direction, the children most advanced in height were not at the same time the heaviest. All combinations occurred, from extreme obesity in children of average or even slightly subnormal size

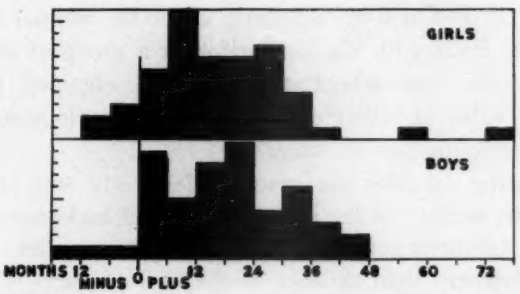

Fig. 7.—Differences in months between height age and chronologic age.

(case 50, table 5, and case 51, table 6) to moderate obesity associated with eminent tallness (case 12, table 5, and case 37, table 6).

SKELETAL MATURATION

In dealing with problems of growth, one has to differentiate clearly between growth in dimension and structural differentiation. Maturation does not necessarily correspond with stature and weight. Progress in maturation is less subject to fluctuation than growth in height and gain in weight. The maturation level for a given age, however, may show a wide range.

The maturation level can be assessed from the structural progress in skeletal development as visualized in roentgenograms. The parts of the skeleton in which cartilage is transformed into bone present the most easily identifiable criteria for assessment. I followed the prin-

18. Czerny and Keller.[1] Rosenstern.[2] Footnote 3.

ciples laid down by Todd in his book on skeletal maturation;[19] before his book became available the standards provided by Flory [20] had been used. Roentgenograms rated according to the latter standards were rerated later, and the average of the two assessments was used as the index of skeletal age. This part of the study was carried out with the cooperation of Dr. Richard Day. All records were rated independently by both of us; our rating agreed generally within a range of plus or minus six months.

Roentgenograms of the hands and wrists of 24 boys and 33 girls were obtained; in a number of cases, roentgenograms showing other parts of the skeleton were taken; these generally corroborated the assessment made from the hand or even showed more advanced development. In tables 5 and 6 only the rating for the hand is given. The degree of maturity as judged from the bone development given as typical by the two standards is designated as "skeletal age." This figure merely indicates the mean value which has been chosen as typical for a given age; it does not say anything about the normal range. This study concerns itself with the comparison of a group of obese children with normal ones from whom standards were obtained, not with the question of whether an individual child shows a development which falls within or outside the normal range.

In comparing data for the group under study with the standards, one has to take account of the influence of social background on skeletal maturation. Children coming from poor homes are less advanced in skeletal development than children of the well to do.[21] The standards of Todd and Flory are based on the study of a selected, well cared for group of children. Todd found that children coming from homes at or near the poverty level may be so affected by their environment as to show a maturation as much as twelve months below that of his standard group. He advised examiners dealing with a group of underprivileged children to use a correction for the assessment of their maturity level. No such correction was used in my study, although the majority of the children came from poor homes. The significance of any finding of skeletal acceleration in obese children is thereby enhanced.

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19. Todd, T. W.: Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937.

20. Flory, C. D.: Osseous Development in the Hand as an Index of Skeletal Development, Monograph of the Society for Research in Child Development, National Research Council, 1936, vol. 1, no. 3.

21. Stettner, E.: Ueber die Beziehung der Ossifikation des Handskeletts zu Alter und Längenwachstum bei gesunden und kranken Kindern von der Geburt bis zur Pubertät, Arch. f. Kinderh. **68**:342, 1921.

The graphic illustration of the relation between skeletal and chronologic age is presented in figure 8, which is constructed similarly to figure 5*A* and *B*. The two lines parallel to the 45 degree line allow for the analytic error of six months in the assessment. Values for the skeletal maturation of 9 boys and 7 girls fall within this zone; those of 1 boy and 1 girl are below it. All others are more or less advanced. The most accelerated growth was that of girls who had undergone early puberty and had started to menstruate before the tenth year. But acceleration of several years was observed also in children who did not yet show any signs of puberal development.

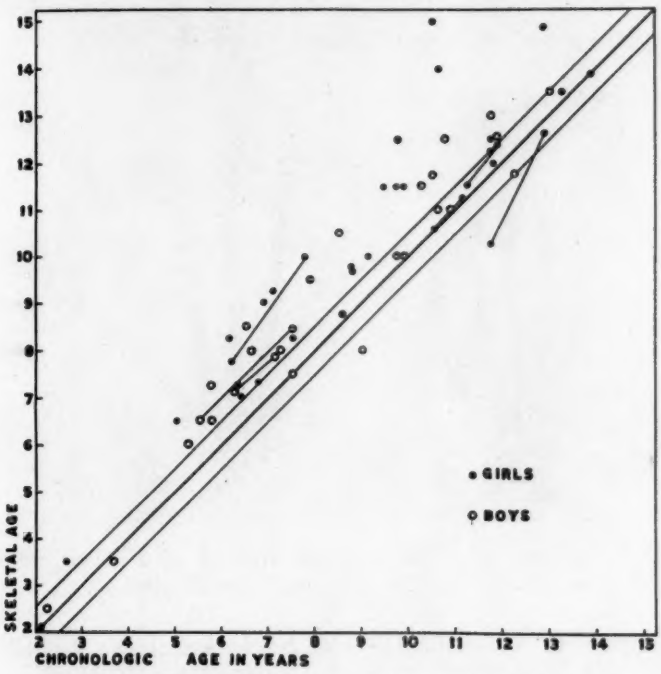

Fig. 8.—Skeletal age compared with chronologic age.

The roentgenogram of the hand of an Italian girl 7 years and 1 month (case 17, table 6) is given as an illustration, together with that of the hand of a normal 7 year old girl (fig. 9). The obese child weighed 9½ pounds (4,309 Gm.) at birth and had been stout since infancy. She did not exhibit any secondary sexual characteristics when the roentgenogram was taken, and none developed during the following year. When the diet was restricted she responded with a satisfactory loss of weight. Comparison of the two pictures shows the advanced maturation of the obese child in several features. The size of the bones is greater; the radial and ulnar epiphyses are more mature, and

the styloid of the ulna is mineralized. The epiphysial heads of the metacarpal bones are broader and are flat on their diaphysial side, while they are still rounded in the hand of the control. The sesamoid bone of the first metacarpal bone is present in the hand of the obese child and absent in that of the control. All these features are consistent with the skeletal development of a normal girl 10 to 11 years of age. The roentgenogram (fig. 10) of the pelvis of a negro girl (case 43, table 6) 10 years and 7 months old illustrates the degree of maturation found in another part of the skeleton. This girl commenced to menstruate when only 9 years old. The maturation of the pelvis as measured by the secondary ossification centers in the crests of the iliums indicates a developmental age of 15 to 17 years.

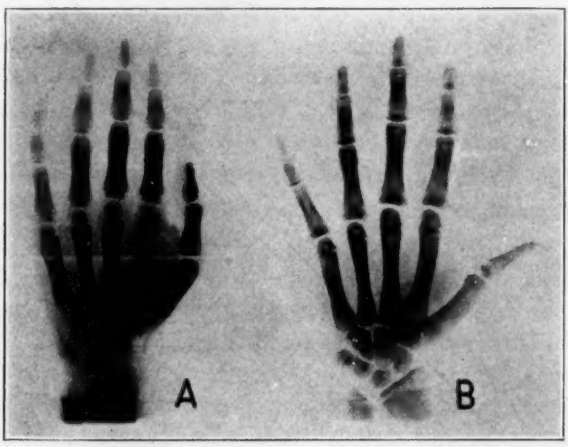

Fig. 9.—Roentgenogram of the hand and wrist, *A*, of a 7 year old normal girl, and *B*, of an obese girl of the same age (case 17, table 6).

A comparison of skeletal age with height age shows that all combinations may occur (fig. 11). In a large group the degree of acceleration was approximately that represented by the values which fall within the range of equality (those of 13 boys and 14 girls). Nine girls were more advanced in skeletal than in statural development; the greatest relative advancement was again found in those who had sexually matured early. Only 1 boy falls into that group. The opposite finding, growth in stature exceeding skeletal maturation, was observed in 10 boys and 8 girls.

In a few cases serial measurements of skeletal maturation were obtained. In figures 8 and 11 the marks relating to these children are connected by lines. The number of cases is too small and the clinical picture too variable to allow more than tentative interpretations. Serial

examinations and comparison of weight, height and skeletal development with sexual maturation will help to explain what connection exists

Fig. 10.—Roentgenogram of the pelvis of an obese Negro girl aged 10 years and 7 months (case 43, table 6).

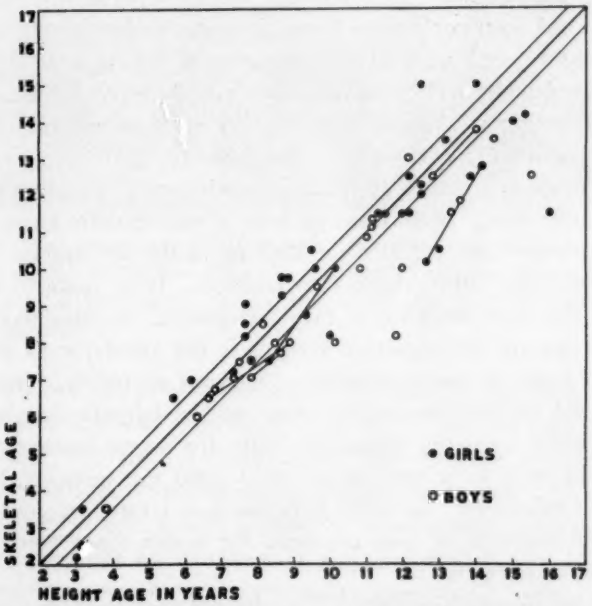

Fig. 11.—Skeletal age compared with height age.

between the excessive height of the obese child and the frequently short stature of the adipose adult, who may present at the same time a dispro-

portion in the development of trunk and extremities, frequently preserving more infantile relations. It seems reasonable to consider this status as resulting from differences in the rates of growth and maturation; accelerated maturation may terminate growth in stature before the person has achieved what otherwise would be his full height. The practical importance of a clear understanding of these relations lies in the circumstance that the use of potent endocrine products may further accelerate skeletal maturation and cause early closure of epiphysial lines, with the result that the final stature may fall short of what the person might have achieved if left untreated.

SEXUAL MATURATION

The number of patients who were at the age of pubertal development is small. Tables 5 and 6 contain one column each referring to the status of sexual development.

One boy showed undescended testes (case 2, table 5); he has been treated, without success up to the time of writing, with large amounts of gonadotropic substance from the urine of pregnant women (follutein, Squibb) for more than a year. It seems likely that in this case a mechanical obstacle rather than glandular dysfunction is the true cause of cryptorchism. On another patient (case 49, table 5) orchidopexy had been performed before he came under my observation; he underwent normal puberal development at the age of 14 years, having received additional treatment with gonadotropic substance from the urine of pregnant women (antuitrin S) after operation. He continued to be markedly overweight after puberty.

For 10 boys the status of sexual development was described as incomplete descensus. In all these patients at one or more examinations one or both testes were found to be high up in the scrotum or inguinal canal but could be pushed down into position. It is doubtful whether in any case this represented true maldevelopment. In the majority of cases this occasional incomplete descensus is not an abnormal anatomic condition so much as the expression of nervous excitability and hyperactivity of the cremasteric reflex. Fear of the parents that the child may not develop normally frequently calls for active therapy. These patients react well to a few injections (1,000 rat units or less) of gonadotropic substance. In table 5, patients so treated are designated. The artificial increase in size prevents the testes from retracting as easily as they did before.

In 29 cases, in which neither size nor position of the testes indicated retardation in sexual development, the status was described as normal. This group comprises also subjects in whom the size of the genitals was masked by excessive fat in the suprapubic region. It is difficult or impossible to judge the outlook for sexual maturation from the size

of the testes during childhood, since they change little in size during the first decade after birth and remain small throughout childhood.[22] Only if the expected increase in size fails to occur after the age of 11 or 12 years is one entitled to suspect or to make the diagnosis of hypogenitalism. In 3 instances (cases 31, 36 and 38, table 5) in which the sexual organs were so small that fear of sexual underdevelopment, rather than concern over the degree of obesity, had brought the patients to the clinic, spontaneous development was observed within a few months; all 3 boys were between 11 and 12 years of age at that time. Figure 12 demonstrates the degree of change in the outer appearance of the reproductive organs in case 31. The patient was an Irish boy who was 11 years and 9 months old and 84 per cent overweight when

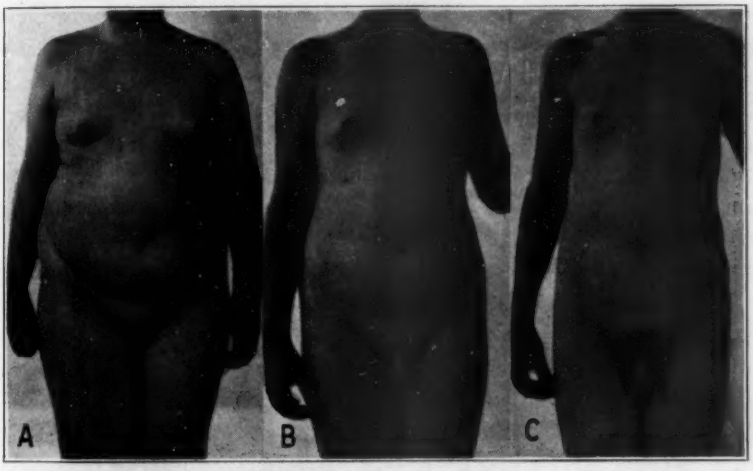

Fig. 12.—Spontaneous sexual development of patient G. T. (case 31, table 5): *A*, on March 5, 1937, at the age of 11 years and 9 months; *B*, on Sept. 7, 1937, at the age of 12 years and 3 months, and *C*, on May 28, 1938, at the age of 12 years and 11 months.

the first picture was taken; the second photograph was made six months later, after he had lost 39 pounds (17.7 Kg.) and was only 30 per cent overweight. The third picture, taken eight months after the second, shows that this boy subsequently attained early puberty; he is listed among the boys who reached puberty while under observation. One boy (case 50, table 5) exhibited at the age of 12¾ years no evidence of spontaneous growth of the genitalia; unfortunately he could not be followed in the clinic, so that nothing is known about his subsequent development.

22. Greulich, W. W., and others: A Handbook of Methods for the Study of Adolescent Children, Monograph of the Society for Research in Child Development, National Research Council, 1938, vol. 3, no. 2, p. 62.

The onset of puberty in boys lacks such an obvious sign as the beginning of menstrual flow in girls. Observation of spermatozoa in morning specimens of urine would be a comparable index. Such a study has been carried out only once, by Baldwin;[23] it certainly would not be a practicable method for a group of boys observed in the outpatient department. The growth of axillary hair, which first makes its appearance after the pubic hair is fairly well developed, seems to be a fairly reliable index of attained sexual maturation.[24] I used this criterion, together with the obvious sign of increased growth of the genitals, for the patients listed as having attained puberty while under observation. Of 15 boys who were between 11 and 14 years of age, 8 had reached this stage of development. This figure does not include 2 of the previously mentioned boys with spontaneous growth of seemingly hypoplastic genitals. Five of the boys who attained early puberty were of Jewish origin; 1 each was of Spanish, Dutch or Irish descent.

The absolute number of observations is too small for any definite conclusions to be drawn; thus far they are in agreement with the statement of Nobécourt, who found normal, sometimes even early, sexual development in obese boys. The fact that more than 50 per cent of the boys in the pertinent age group reached puberty before the age of 14 years should raise doubt concerning the concept that obesity in boys is a concomitant manifestation of hypogenitalism. It may be that circumstances are different for boys who grow fat during adolescence. Only persistent follow-up studies on a critically observed group will give more definite information.

One additional point must be considered in this connection: the fact that gynecomasty is encountered not infrequently in these boys, which seems to corroborate the concept of sexual maldevelopment. In my experience, however, it merely indicates a local accumulation of subcutaneous fat tissue in the mammary region. In no case did I observe a simultaneous swelling of the areolas, development of glandular tissue, lactation or any other findings suggestive of a development of female characteristics. The mammary region is one of the sites of predilection for deposits of fat. They are observed in a similar form in little girls long before any signs of beginning puberal development are noticed. The boys who showed this symptom have not been enumerated in detail. That the condition may persist for some time after an early and in no way inadequate genital development has commenced is illustrated by

23. Baldwin, B. T.: The Determination of Sex Maturation in Boys by a Laboratory Method, J. Comp. Psychol. **8**:39, 1928.

24. Godin, P.: Récherches anthropométriques sur la croissance des diverses parties du corps, ed. 2, Paris, Amédée LeGrand, 1935.

patient 31 (fig. 12). In this case gynecomasty, which had been a distressing disfiguration since early childhood, disappeared only after the weight had become normal.

In grouping the girls, I have used four different designations for the description of the state of sexual maturation: "normal," "pseudobreast formation," "prepuberty" and "menstruation." Reference is made to the state of development at the time when last seen, not at first examination. The term "normal" is used for girls whose state of development was in agreement with their age; since the girls were very young, it indicates the absence of secondary sexual characteristics.

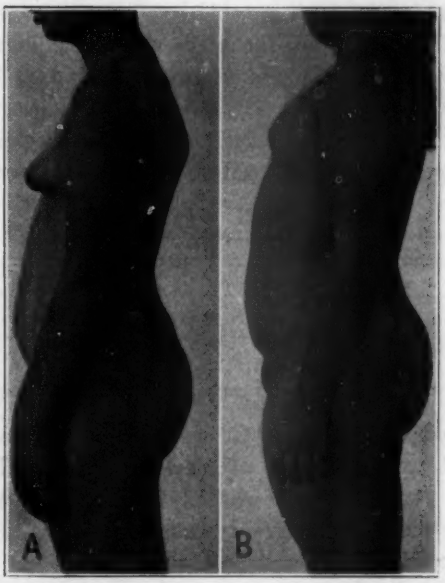

Fig. 13.—*A*, puberal development of breast (case 37, table 6; age 9 years and 9 months); *B*, pseudodevelopment of breast (case 29, table 6; age 9 years and 2 months).

Twenty-three girls comprised this group, only 1 of whom was more than 10 years old (case 41, table 6); all others were younger.

In addition, there were 10 girls who did not show any true signs of puberal development but who had deposits of fat in the mammary region which simulated a more or less mature breast. This condition is designated as "pseudobreast" in the table, since it lacks the changes observed in the truly maturing breast. The papilla presents the same picture as in the infantile breast; it is only slightly elevated above the disk-shaped areola. Figure 13 illustrates the different types of breast formation (cases 29 and 37, table 6). The oldest girl in this group was 11 years and 7 months old (case 46) and the youngest 2 years

(case 1). In the case of 1 girl (case 8) precocious sexual development had been suspected when she was 5½ years old. She did not return to the clinic before the age of 10½ years. The breasts and the pubic and axillary hair were well developed at that time, but the menarche had not yet occurred. It cannot be judged from the record whether it was such an accumulation of fat in the mammary region which led to the earlier suspicion of precocious puberal development. This girl was later a member of the group of 10 girls who exhibited signs of approaching puberty but had not yet commenced to menstruate. In 8 girls the menarche occurred before they were 13 years old. The age distribution for development of secondary sexual characteristics and onset of menstruation is given in table 7.

The racial distribution of the girls who were menstruating is as follows: Four were Jews, 2 were white Americans of North European descent, 1 was Hungarian and 1 was American Negro.

The time at which the menarche occurs is determined by various factors. The figures given by different authors cover a wide range.

TABLE 7.—*Puberal Development of Obese Girls*

Age, years	8	9	10	11	12	13
Girls undeveloped	11	3	1	1	..	..
Secondary characteristics developed	1	4	2	2	1	..
Girls menstruating	..	2	1	2	1	2

Engle and Shelesnyak [25] based their study on observations of 250 girls in the Hebrew Orphan Asylum of New York city. The average age at the menarche for that group was 13½ years, with a range of 11 to 16.3 years. The menarcheal age of obese girls is unquestionably lower, and in a number of cases it falls below the lower limit of the normal range. This behavior is in agreement with the findings of other authors,[26] who also observed that puberty occurs early in obese girls.

Though the present article deals with the physical aspects of growth and development of the obese child, I wish to point out that the mental development, as expressed by the intelligence quotient, is frequently advanced. Mental development, together with the rate of physical growth and maturation, is used as a guide in treatment of children suffering from hypothyroidism.[27] One may speculate whether the high intelligence quotient in obese children is an expression of greater mental

25. Engle, E. T., and Shelesnyak, M. C.: First Menstruation and Subsequent Menstrual Cycles of Pubertal Girls, Human Biol. **6**:431, 1934.

26. Hering.[3d] Ellis and Tallerman.[5] Nobécourt.[10] Bornhardt.[11]

27. Wilkins, L.: Rates of Growth, Osseous Development, and Mental Development in Cretins as a Guide to Thyroid Treatment, J. Pediat. **12**:429, 1938.

endowment or merely an index of a faster rate of development. An extensive discussion of the mental development of obese children will be given in another article.

COMPARISON WITH LONGITUDINAL OBSERVATIONS ON NORMAL CHILDREN

Reviewing the presented data, it may be stated that these obese children are advanced in stature; their skeletal development is average and sometimes accelerated; early sexual maturity is the rule for obese girls and is not uncommon in obese boys. Similar relations between rate of increase in height and weight and sexual maturation have been observed in large groups of normal children. Richey [28] reported observations made in the Laboratory Schools of the University of Chicago on more than 3,600 children. Height and weight were recorded as well as the status of sexual development on successive birthdays throughout the school period, from the age of 6 to the age of 17 years. The collected data were later arranged according to the age at onset of puberty. The whole group was divided into three maturity groups each for boys and girls. The three groups for boys refer to the onset of maturity (the appearance of axillary hair being used as a criterion) at or before 14 years, between 14 and 15 and at or after 15. The data for girls were arranged (according to onset of menarcheal flow) at or before 13 years, between 13 or 14 and at or after 14.

In order that differences might be demonstrated more clearly, the same boys were divided into five groups, the youngest group maturing at or before 13 years and the oldest at or after 17 years. Figure 14 is based on data obtained in Chicago and published in another form by Richey. *A* shows the average height curves for girls of maturity, groups I and III. The values for group II would fall somewhere between these two curves. Girls who are going to attain puberty at an earlier age are taller throughout the growth period than those who will mature later. But their curve levels out after puberty and is crossed by the curve of girls who mature later. The heights of the obese girls would distribute themselves above and below curve I. This indicates that the height development of obese girls is in harmony with the growth in stature of normal children of the same menarcheal age.

The curves for the boys divided into three groups are similar. There are no significant differences in the heights of the different groups after the age of 17 years. The subdivision into five groups enlarges the differences during the growing period between boys who mature

28. Richey, H. G.: Relation of Accelerated, Normal and Retarded Puberty to the Height and Weight of School Children, Monograph of the Society for Research in Child Development, National Research Council, 1937, vol. 2, no. 1.

early and those who mature late. Only three of the five curves are given in figure 14 *B*. The heights of obese boys would fall between curves I and III, corresponding to the height of normal boys of a comparable maturity level.

Since the children who mature early are taller throughout childhood, it seems only logical to expect them to be heavier also. This expectancy is confirmed by the actual observation. But the differences in weight are in excess of what would be predicted from the difference in height

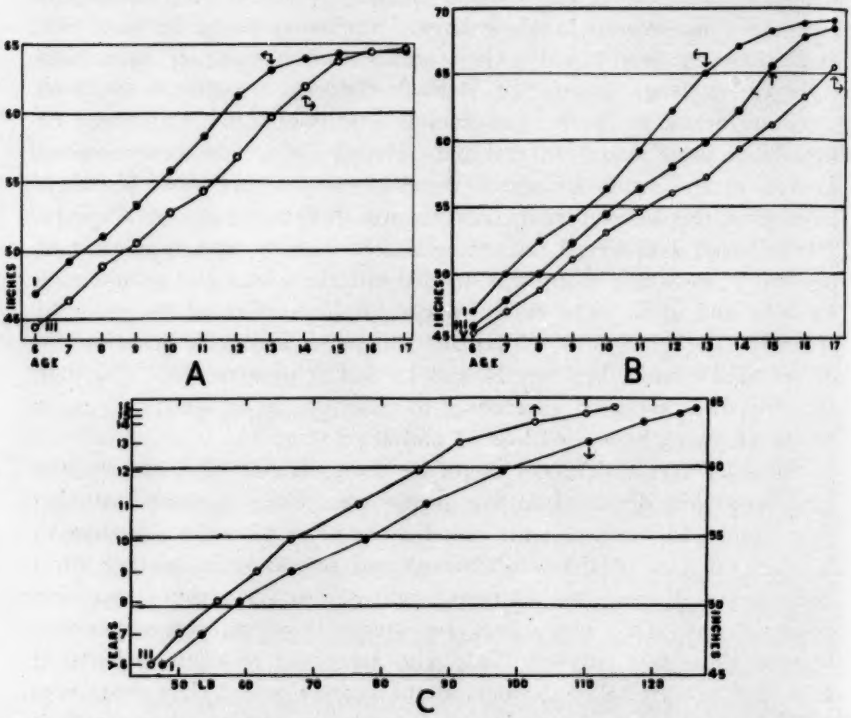

Fig. 14.—*A*, average heights of girls maturing *I*, at or before the age of 13 years, and *III*, at or after 14 years. *B*, average heights of boys maturing *I*, at or before 13 years; *III*, at 15 years, and *V*, at or after 17 years. *C*, weights of girls maturing *I*, at or before 13 years and *III*, at or after 14 years, given for the average heights of all groups.

alone. Even if the difference in height is completely neglected, the average weights for the groups maturing early are higher than for those maturing late. This circumstance is illustrated in figure 14 *C*, which gives curves representing the average weight for the girls of maturity groups I and III, for the average height of all groups. The differences are noticeable throughout; in contrast to the difference in height, they persist after puberty and cessation of growth. A girl who

matures early is on the average 18 pounds (8.2 Kg.) heavier at 13 years than a girl of the same age and height who matures late. The course of weight development in boys is similar. If the actual differences in height are taken into account, the absolute excess in weight of the groups maturing early will be even more obvious.

This variation of the height and weight of children with their state of biologic development is not considered in the ordinary height-age-weight tables, such as those of Baldwin and Wood. Deviations from the so-called ideal weight can be properly appraised only if the degree of sexual maturation is taken into account.

The weights of all obese children presented in this study are much greater than those observed in Richey's study of the groups maturing early. The condition of the obese children manifests an exaggeration of a developmental trend observed in normal children; the difference is only quantitative and points to a fundamental similarity in the relations between the different factors representing progress in growth and maturation.

Evaluation of the advancement in skeletal maturation was attempted in a similar way by comparison with observations obtained in serial studies of normal children. The work of Shuttleworth [29] deals extensively with these relations of physical growth and sexual maturation. The reports published thus far are limited to observations on girls. Shuttleworth's material is divided into eight menarcheal groups. The findings with regard to height and weight development of girls are in agreement with the results obtained by Richey for both sexes. A strict parallelism was found to exist between sexual maturation and skeletal development, i. e., girls who were going to menstruate early were further advanced in skeletal maturation than those in whom the menarche was to occur at a later age. I am not familiar with a study reporting similar circumstances for boys. However, observations on precocious puberty [30] suggest that a close correlation exists between early puberal maturation and advanced ossification for both sexes alike.

Like accelerated growth in stature, advanced skeletal maturation is a sign of increased rate of general development, which also expresses itself in early advent of puberty and greater weight.

COMMENT

The similarity in the growth pattern of obese children and normal children who mature early suggests that fundamentally no difference

29. Shuttleworth, F. K.: Sexual Maturation and the Physical Growth of Girls Age Six to Nineteen, Monograph of the Society for Research in Child Development, National Research Council, 1937, vol. 2, no. 5.

30. Neurath, R.: Die Pubertät: Physiologie, Pathologie, Vienna, Julius Springer, 1932, p. 96.

exists in the laws regulating the growth of obese and of normally nourished children.

Gross size at a given age should be regarded as the momentary status in the growth pattern of numerous single elements which make up the whole organism and which, because they have a certain degree of independence, may produce widely different types of body build. Studies on longitudinal growth have elucidated the growth trends in homogeneous groups of children from age to age. With the aid of such curves, one may attempt to predict the growth trend of an individual, such as an obese child, whose aspect differs markedly from the normal average and yet whose growth processes may be governed by the laws that apply to the average child at a comparable stage of development.

The factors which are responsible for individual differences in growth are numerous and frequently ill defined; only a few which appear to be of importance for growth in obese children will be discussed in this paper.

The power of growth and differentiation is an intrinsic quality of each living organism. The individual follows a hereditary pattern; this includes not only the specific intensity of growth, which may vary widely for different structures at different times, but the duration of the individual periods of growth. These factors may be conditioned by internal and external influences; among the first, the role of the endocrine system is recognized, although its importance has probably been overemphasized; among the environmental factors, the importance of nutrition has been widely studied and is obviously of material significance in the growth problems of obese children.

Most of the reported work in this field has been concerned with the influence of quantitatively or qualitatively insufficient nutrition. The long-continued undernutrition of the youth of Central Europe during the Great War[31] manifested itself not only in deficient weight but in severe statural retardation and marked delay of puberal development.

It is doubtful whether dietary supplements can raise the intensity of growth above the rate of the inherited growth pattern. Some workers have held the view that the effectiveness of a dietary supplement serves only to prove that the previous diet had not been optimal. The recent work of Roberts and her co-workers[32] showed that the addition

31. Schlesinger, E.: Das Wachstum des Kindes, Ergebn. d. inn. Med. u. Kinderh. **28**:535, 1925.

32. Roberts, L. J.; Blair, R.; Lenning, B., and Scott, M.: Effect of a Milk Supplement on the Physical Status of Institutional Children: I. Growth in Height and in Weight, Am. J. Dis. Child. **56**:287 (Aug.) 1938. Previous work by British and American authors is quoted in this article. MacNair, V., and Roberts, L. J.: II. Ossification of the Bones of the Wrist, ibid. **56**:494 (Sept.) 1938.

of 1 pint of milk to a not grossly insufficient diet could in the course of a year significantly increase the growth in height and weight and the rate of skeletal differentiation.

The importance of the normal function of the endocrine glands, especially of the thyroid and the pituitary gland, for normal progress of growth and development is firmly established through clinical and experimental evidence.[33] Lack or insufficient supply of either hormone is associated with retardation in dimensional growth and maturation; in hypothyroidism the mental development also is greatly retarded. The dominant position of the pituitary gland in regulating growth and stimulating maturity is well known. The administration of potent pituitary preparations may lead to precipitate maturation and produce pictures resembling precocious puberty.[34] Shuttleworth attributed the different rates of physical development of girls to underlying biologic, and presumably endocrine, factors which begin to operate at an early age in some children and later in others.

The reported findings on obese children are in harmony with the observations that abundant nutrition intensifies the rate of growth. The food intake of the obese child is so high above his needs that after the energy for a rapid rate of growth has been supplied the excess is stored as subcutaneous fat. In addition to the capacity for storage, it may well be that a specific capacity for growth, which can be called into play by excessive nutrition, is inherited by these children and that this endowment for early development represents what is frequently referred to as the constitutional factor. It is questionable, however, whether this development at the fastest possible rate is justly called optimal.

The course of growth and development in obese children, which one may describe as the reverse of infantilism, cannot be brought into agreement with the well defined picture of hypothyroidism, nor can it be correlated with hypopituitarism, so far as there are means of estimating its relation to growth and development. It is not reasonable to explain accelerated development as resulting from hypofunction of glands the growth-promoting qualities of which are as firmly established as those of the thyroid and the hypophysis. Nothing in this study of the obese child, on the other hand, warrants an interpretation of hyperfunction of either gland. The function of the endocrine glands is only one factor among numerous others which affect the individual pattern of growth; not every variation in the chronologic evolution of the growth pattern should be classified as an endocrine dysfunction.

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33. Aldrich, C. A.: Growth and Development: The Endocrine Glands and Growth, J. Pediat. **6**:392, 1935; The Endocrine Glands and Growth: The Thyroid, ibid. **8**:381, 1936.

34. Thompson, W. O., and Heckel, N. J.: Precocious Sexual Development from an Anterior Pituitary-like Principle, J. A. M. A. **110**:1813 (May 28) 1938.

Although obesity in childhood is a distressing condition, obese children differ only quantitatively in their physical make-up from the numerous possible patterns due to individual variations in growth. The rhythm of their growth is disturbed; it is not abnormal in a qualitative way.

Therapeutic measures should avoid everything which may lead to further stimulation of the already active processes of growth and maturation. The careful therapeutist must direct his attention toward control of diet; this constitutes at present the most accessible external factor with properties of promoting growth and weight which are clearly recognized.

SUMMARY

Growth and maturation of 102 obese children, 2 to 13 years of age, are compared with results obtained in studies of normal children.

Growth in stature is in excess of the average normal but in harmony with the height development of children who mature early. Skeletal maturation is normal or advanced, certainly not delayed.

The menarche in obese girls occurs early, in several instances before the age of 10 years. More than 50 per cent of the boys between 11 and 14 years old show signs of approaching or attained puberal development.

Since the weight of normal children who mature early is significantly higher than that of children who mature later, the high weight of the obese child can be considered as an exaggeration of a normal trend.

The findings of intensive growth and early maturation are not consistent with theories which attempt to explain obesity on the basis of hypothyroidism and hypopituitarism; they agree with observations of the growth-promoting effect of abundant nutrition.

ENTEROGENOUS INTRAMURAL CYSTS OF THE INTESTINES

DANIEL J. PACHMAN, M.D.
CHICAGO

Enterogenous cysts have been found in close relation to almost every portion of the intestinal tract. They have occurred also outside the abdomen, chiefly in the mediastinum.[1] These cysts usually duplicate the layers and the mucosa of the intestine from which they are derived and may in this manner be differentiated histologically from other cysts, such as those of dermoid or lymphatic type. The appearance of the epithelial lining of the cystic cavities may vary considerably, since distention and inflammatory reactions may cause changes. Glands resembling those present in the intestine are often noted in the submucosal layer.

The largest number of cysts of enterogenous origin have been found in the region of the obliterated omphalomesenteric duct. For this reason, many authors have stated the belief that these cysts are derived from remnants of this structure. They are considered closely related, then, to Meckel's diverticulum. The latter may be a stage in the transformation of such a cyst, from a pouch having direct continuity with the lumen of the bowel, to a structure which is entirely independent of the intestinal lumen (fig. 1). Such a theory does not adequately explain the appearance of enterogenous cysts in positions far removed from the site of origin of the vitelline duct, such as the mediastinal, duodenal [2] and rectal [3] regions.

From the Department of Pediatrics, University of Chicago.

1. (*a*) Roth, M.: Ueber Missbildungen im Bereich des Ductus omphalomesentericus, Virchows Arch. f. path. Anat. **86**:371, 1881. (*b*) Poncher, H. G., and Milles, G.: Cysts and Diverticula of Intestinal Origin, Am. J. Dis. Child. **45**:1064 (May) 1933. (*c*) Black, R. A., and Benjamin, E. L.: Enterogenous Abnormalities: Cysts and Diverticula, ibid. **51**:1126 (May) 1936.

2. (*a*) Sänger, M., and Klopp, A.: Zur anatomischen Kenntnis der angeborenen Bauchcysten, Arch. f. Gynäk. **16**:415, 1880. (*b*) Meyer, C.: Ein Beitrag zur Kenntnis der Enterocystome in Säuglingsalter, Ztschr. f. Kinderh. **21**:272, 1919. (*c*) Waugh, O. J.: Congenital Cyst of the Duodenum, Surg., Gynec. & Obst. **37**: 785, 1923. (*d*) Maddox, K.: Cyst of the Duodenum Simulating Pyloric Obstruction, M. J. Australia **1**:900, 1927. (*e*) Smith, R. E.: A Case of Enterocystoma of the Duodenum Simulating Pyloric Stenosis, Guy's Hosp. Rep. **80**:463, 1930. (*f*) Gardner, C. E., Jr., and Hart, D.: Enterogenous Cysts of the Duodenum: Report of a Case and Review of the Literature, J. A. M. A. **104**:1809 (May 18) 1935. (*g*) Basman, J.: Enterogenous Cyst of the Duodenum Simulating Pyloric Stenosis, J. Pediat. **12**:363, 1938.

3. McLanahan, S., and Stone, H. B.: Enterogenous Cysts, Surg., Gynec. & Obst. **58**:1027, 1934.

In view of the occurrence of cysts in these regions, it appears likely that enterogenous cysts can also be derived from sequestration of embryonal intestinal epithelium early in fetal life. In such a case this tissue later develops and forms the nucleus of the cyst. Hughes-Jones [4] sectioned human embryos and could demonstrate islands of epithelial tissue similar to that of the intestine lying in close relation to, but not within, the intestinal wall. He expressed the belief that this tissue might be the origin of some cysts. Lewis and Thyng [5] found numerous

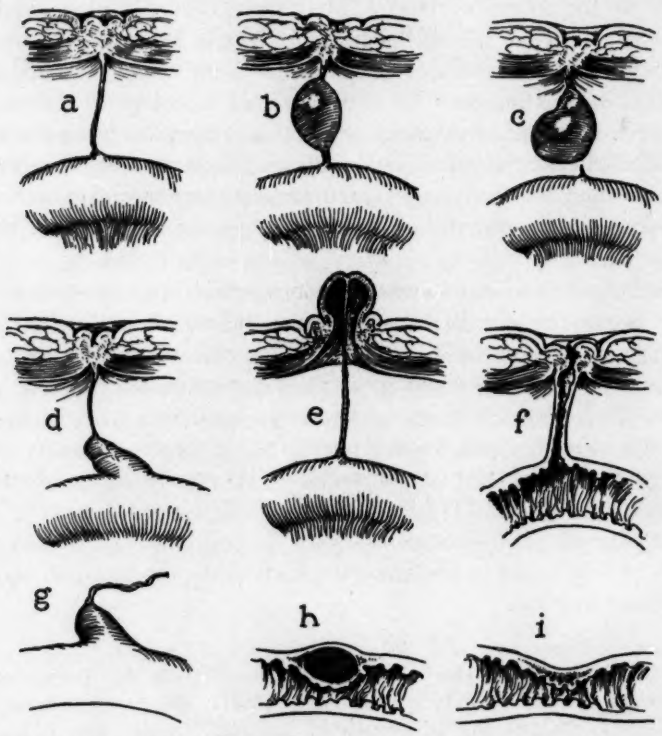

Fig. 1.—Diagrammatic representation of structures derived from remnants of omphalomesenteric duct: *a*, cord extending between umbilicus and ileum; *b*, cyst suspended between umbilicus and ileum; *c*, cyst suspended from umbilicus; *d*, Meckel's diverticulum with cord extending to umbilicus; *e*, everted mucocele attached by cord to ileum; *f*, fecal fistula between ileum and umbilicus; *g*, Meckel's diverticulum with free intraperitoneal cord; *h*, enterocystoma; *i*, stenosis from excessive evolution (illustration and legend from Montgomery, A. H., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Co., Inc., 1937, vol. 3, chap. 6, p. 26).

4. Hughes-Jones, W. E. A.: Enterogenous Cysts, Brit. J. Surg. **22**:134, 1934.

5. Lewis, F. T., and Thyng, F. W.: The Regular Occurrence of Intestinal Diverticula in Embryo of the Pig, Rabbit and Man, Am. J. Anat. **7**:505, 1907.

diverticula of the duodenum and upper portion of the intestine in a human embryo and stated the opinion that these pouches could persist and in some cases become completely separated from the intestine.

Enterogenous cysts have been found most frequently between the layers of the mesentery, in particular that of the ileocecal region. Intramural cysts of similar origin are fortunately far less common. The management of intramural cysts, because of their close relation to the lumen of the bowel, presents a serious problem. This paper is concerned chiefly with such intramural enterogenous cysts. However, it is fully realized that cysts which lie in the mesentery adjacent to the intestinal tract may produce symptoms and signs indistinguishable from those of cysts which lie within the wall of the bowel.

During the last three years, 3 patients under 1 year of age with intramural cysts of the intestine have been seen at the Bobs Roberts Memorial Hospital for Children. From 2 of these children pathologic specimens were obtained, and the cyst in each case was proved to be enterogenous. In the third case no attempt was made to remove any portion of the cyst for histologic examination, but the size, appearance and location of the tumor made its derivation from the intestine most likely.

REPORT OF CASES

Case 1.—C. Z., a girl of 4 months, was first seen in the outpatient department of the Bobs Roberts Memorial Hospital for Children on June 20, 1936. At that time the child had a cold, and the mother stated that there was a "swelling in the abdomen on the right side which comes and goes." She had noted this mass for the first time one month previously.

The child had been delivered spontaneously, weighing 8 pounds and 5½ ounces (3,775 Gm.) at birth. The neonatal period was entirely normal. The infant was artificially fed; she had vomited occasionally after feedings since birth.

At the time of the first visit the child's temperature was 38.2 C. (100.7 F.), and the right ear drum was infected and bulging. An indefinite round mass about 7 by 7 cm. was palpated on the right side of the abdomen. Myringotomy was performed on the right. However, the patient was admitted to the hospital two days later, when vomiting became more severe.

Physical examination revealed a well developed and well nourished infant who did not appear ill. She was not dehydrated and was breathing normally. The right ear was draining a small amount of purulent fluid. Otherwise physical examination showed no abnormality except in the abdomen. Visible upper abdominal peristalsis was present, and a rather tense, nonpulsating mass could be palpated in the right paraumbilical region.

The urine was normal. The white blood cells numbered 10,000, with 40 per cent polymorphonuclears and 60 per cent small lymphocytes.

Roentgen examination of the gastrointestinal tract on June 25 revealed no evidence of obstruction to the passage of barium sulfate from the stomach into the duodenum. There was nothing to suggest a lesion. The duodenal bulb was not well filled in any of the views, but it is difficult to demonstrate a filled bulb in an infant. There was a considerable amount of barium sulfate in the upper part

of the small bowel. No organic lesion was noted in the colon. The ascending colon and the cecum were displaced to the left by a mass of soft tissue on the right side of the abdomen (fig. 2).

An intravenous pyelogram made on June 29, four days later, showed moderate hydronephrosis of the right kidney. However, the degree of hydronephrosis was not considered sufficient to explain the size of the mass.

The child continued to vomit during the entire first week, and an exploratory laparotomy was thought advisable. A tentative preoperative diagnosis of cyst of the abdomen was made. When the abdomen was opened a huge cyst presented itself, and 550 cc. of rather thin, greenish black fluid was slowly aspirated. This had the characteristics of old cystic fluid into which hemorrhage had occurred. Palpation about the base of the cyst indicated that it arose from the duodenum just below the pylorus and that it was not connected with the right kidney. A small piece of the cyst wall was removed for biopsy, and a small catheter was

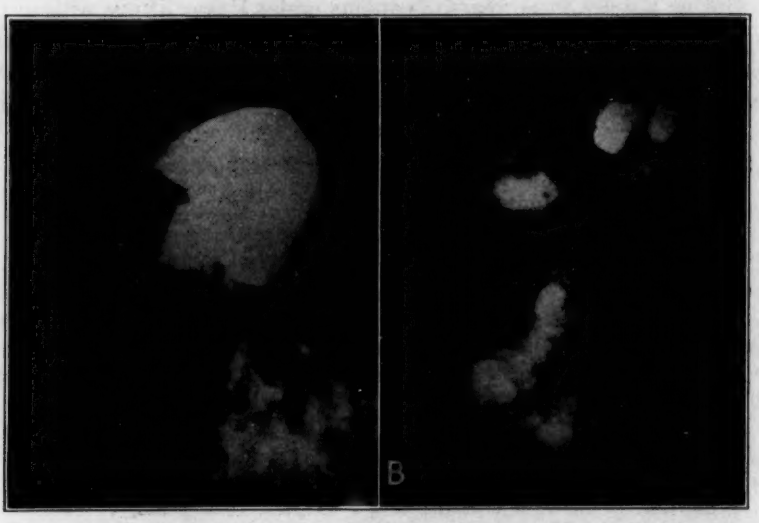

Fig. 2.—*A*, roentgenogram taken a short time after the oral administration of barium sulfate, showing no obstruction to its passage. *B*, roentgenogram obtained after a barium sulfate enema, showing the displacement of the intestines to the left.

inserted and secured to the peritoneal opening. In this manner partial marsupialization was obtained.

During the operation the patient was given a blood transfusion, saline solution intravenously and 100 cc. of Ringer's solution by hypodermoclysis. The child, however, responded poorly and died four hours after the operation.

Autopsy was performed by Dr. P. Steiner, who furnished the following report:

The stomach was moderately distended. One centimeter beyond the thickened pyloric ring the wall of the duodenum was greatly thickened; adherent to this portion was the cyst (fig. 3). No communication could be found between the cyst and the lumen of the duodenum. The cyst was about 8 by 11 cm. and pear shaped. Its wall was firm and was 2 to 4 mm. thick. The duodenum at the pyloric ring measured 4.5 cm. The portion of the duodenum beyond the cyst was

normally thin walled and narrowed to 2 cm. in circumference. The distance from the pyloric ring to the papilla of Vater measured 14 cm., and from the pyloric ring to the cyst the duodenum measured 1 cm. The papilla of Vater was located 6.5 cm. below the distal margin of the cyst. The cyst was therefore in contact with duodenal wall for 6.5 cm. The remainder of the gastrointestinal tract was normal.

Histologic examination of a section of the wall of the duodenal cyst showed a thin, fibrous outer coat and a heavy muscular coat consisting of a thick outer longitudinal layer and an even thicker inner circular layer of muscle. A section

Fig. 3 (case 1).—Photograph of specimen obtained post mortem, showing the duodenal cyst and its relation to the stomach and duodenum.

taken through the duodenum as it approached and became adherent to the cyst showed normal duodenal mucosa and muscular wall. At the junction with the cyst, the outer longitudinal layer of muscle became irregular and was reflected over the cyst. The wall common to the duodenum and cyst showed them adherent or united by their outer longitudinal muscular coats. The cyst in this region was lined by mucosa which resembled that of the duodenum (figs. 4 and 5).

Case 2.—W. M., an 8 month old boy, was admitted to the Bobs Roberts Memorial Hospital for Children on Dec. 9, 1936, the chief complaint being vomiting of two weeks' duration. The family history was noncontributory. The child was born at full term, weighed 7 pounds and 6 ounces (3,345 Gm.) at

birth and had an uneventful neonatal period. He had been fed on an artificial formula and had developed properly. His past history was entirely irrelevant except for a discharge from the left ear at 6 months.

The infant was well until two weeks before admission, when he began to have abdominal pain, characterized by drawing up of his legs and crying. At the onset he vomited a part of his feedings. No fever was noted, and the stools were normal. The following day the child seemed better, vomiting only occasionally. Then the symptoms completely disappeared except for a mild attack of pain and vomiting one week before admission.

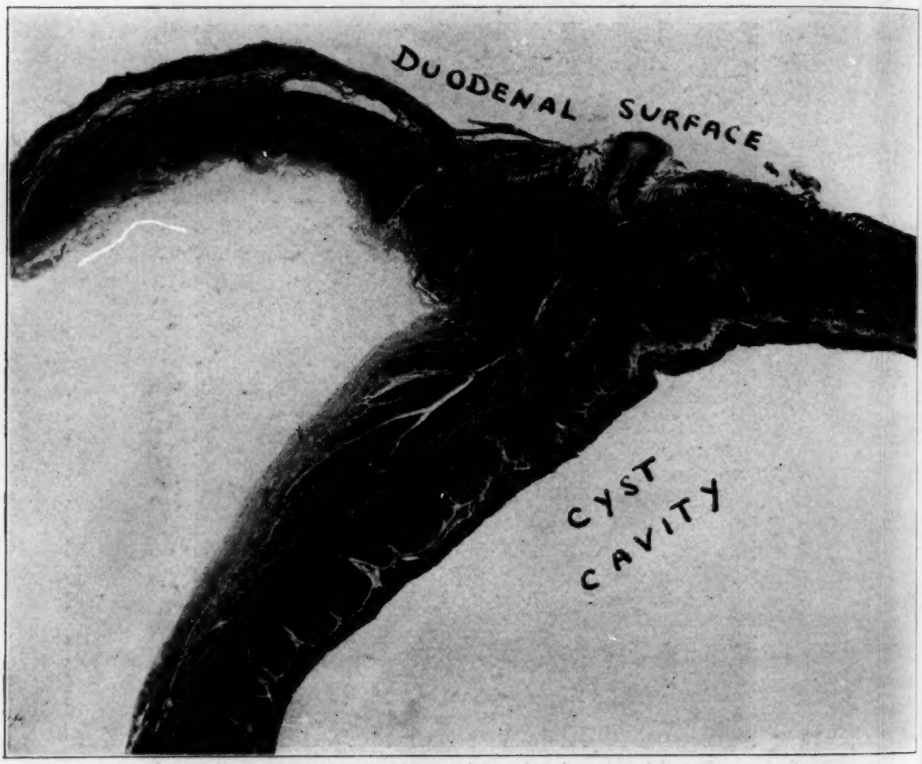

Fig. 4 (case 1).—Low power photomicrograph of a section of the normal duodenum and a portion of the cyst wall.

Two days before the patient's admission the vomiting began again and continued. His bowel movements were constipated. Enemas had been given, and a small amount of fecal material not containing blood was obtained.

Physical examination showed a well developed and well nourished boy who cried intermittently as if in pain. The examination showed essentially normal conditions except in the abdomen. There was no rigidity of the abdominal wall. A sausage-shaped mass was felt in the transverse position above the umbilicus. The rectal examination revealed no abnormality.

Barium sulfate enemas showed some obstruction to the passage of the barium sulfate into the transverse colon. The obstruction, however, gave way under slight

pressure. However, the vomiting continued, and on December 11, two days after the child's admission, an exploratory laparotomy was performed by Dr. L. R. Dragstedt, of the department of surgery. A tumor mass was found in the ileocecal region. An intussusception was present; this was partially reduced. A tensely distended ovoid mass about 1½ inches (3.8 cm.) in diameter was palpated in the ileocecal region. This mass proved to be a cyst within the wall

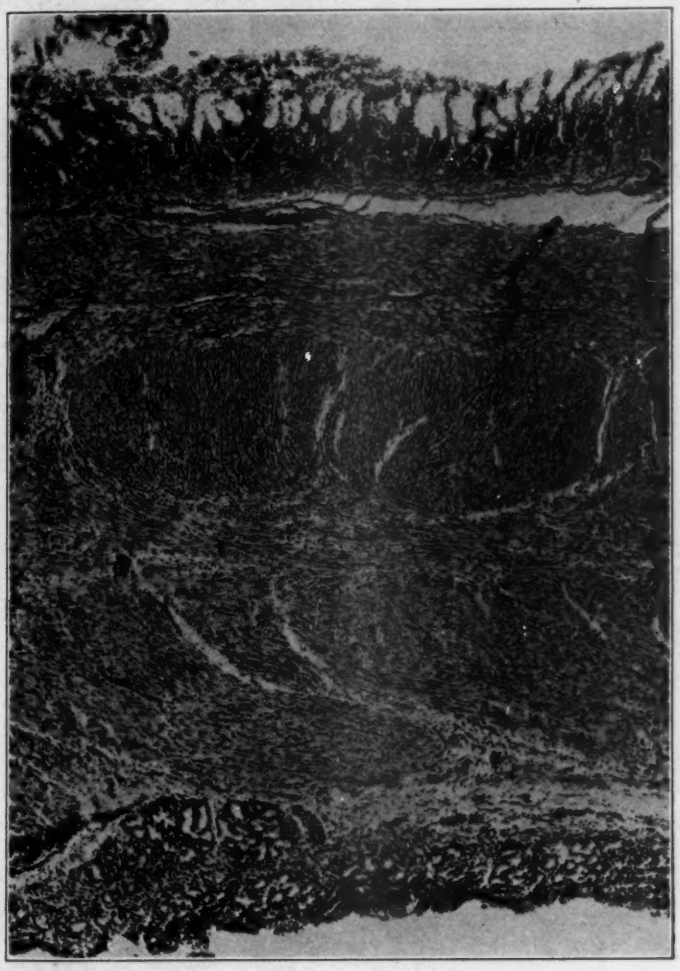

Fig. 5 (case 1).—High power photomicrograph of a section of the cyst wall. The inner layer (the lining of the cyst cavity) closely resembles the outer layer, which is duodenal mucosa.

of the ileum and was removed along with 6 inches (15 cm.) of ileum, cecum and a portion of the ascending colon (fig. 6). A lateral anastomosis between the proximal part of the ileum and the transverse colon was performed. Histologic examination of a section of the cyst wall showed that its structure was similar to that of the intestine (fig. 7 and 8).

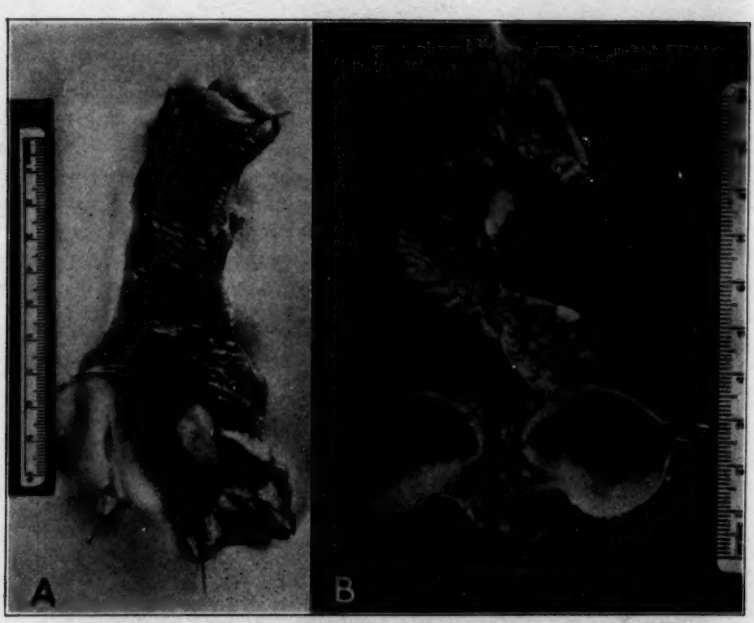

Fig. 6 (case 2).—*A*, photograph of the resected specimen. The intermuscular cyst is seen at the left. *B*, photograph which shows the size and interior of the cyst cavity.

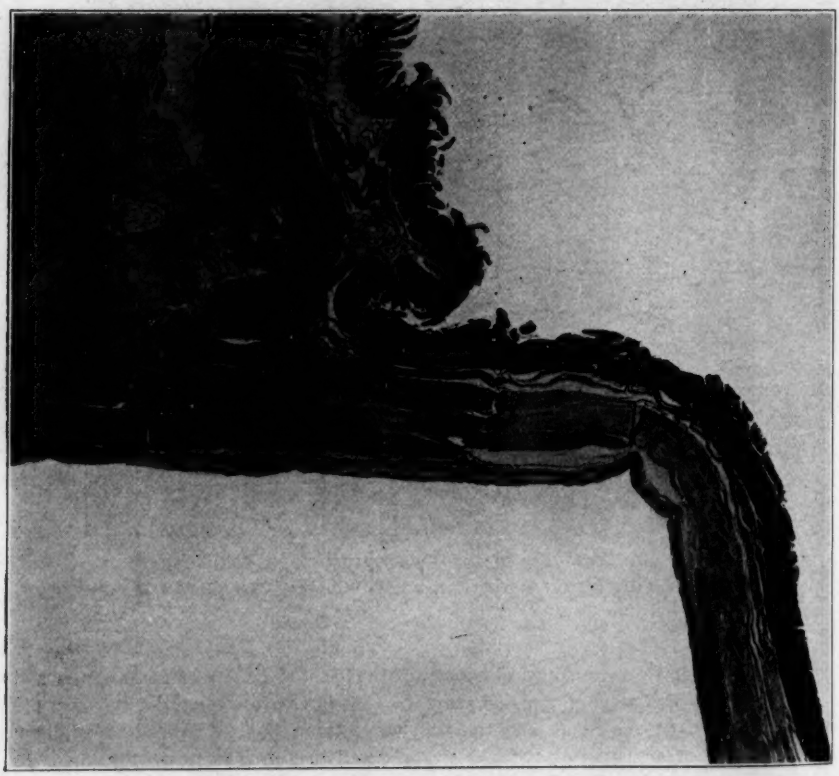

Fig. 7 (case 2).—Low power photomicrograph of a section of the cyst wall and adjacent normal ileum.

The child had a rather stormy postoperative course, complicated by acute dilatation of the stomach. This was relieved by constant gastric aspiration with a nasal tube.

On December 18, nine days after admission, the stools again became normal. The temperature then dropped to 37.2 C. (99 F.), and the patient made an

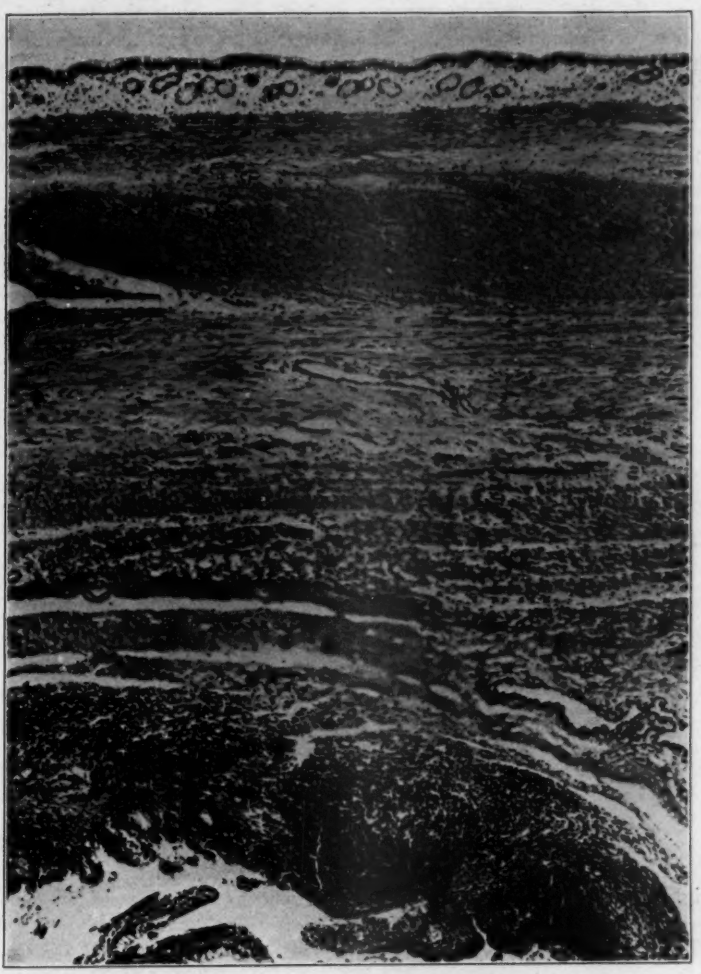

Fig. 8 (case 2).—High power photomicrograph of the cyst wall. Many glands resembling those in the intestine are seen in the mucosa (top layer) lining the cyst cavity.

uneventful and complete recovery, being discharged on December 23, two weeks after admission.

The diagnosis was enterocystoma of the ileum and intussusception, secondary to the cyst.

The infant was again admitted to the hospital on Jan. 4, 1937, twelve days after discharge, because of a recurrence of symptoms. He had been well until

two days previously. At that time he began to vomit his feedings, and he continued to vomit everything he ate. Physical examination showed a moderately ill, mildly dehydrated infant of 9 months. There was a well healed abdominal incision. No abdominal rigidity was present. An indefinite mass was felt in the right upper quadrant. The rectal examination showed no abnormality. A barium enema revealed a complete obstruction in the proximal part of the transverse colon at the site of the anastomosis of the colon with the terminal ileum. Operation revealed intussusception of the ascending colon into the transverse colon, which produced the block obstruction between the distal part of the ileum and the

Fig. 9 (case 2).—Photograph of the patient as he appeared in November 1938, at the age of 2¼ years.

transverse colon. This was reduced, and the end of the ascending colon was sutured to the anterior abdominal wall to prevent further intussusception. The patient had a rather uneventful subsequent hospital course, except for a slight infection of the wound. Vomiting did not recur, the stools again became normal, and the boy was discharged thirteen days after admission.

Since his last discharge the child has done well, has gained weight and has developed satisfactorily. At the time of writing he is 2½ years old, weighs 31 pounds (14.1 Kg.) and is in excellent physical condition (fig. 9). There has been no recurrence of the vomiting, and there are no gastrointestinal symptoms.

CASE 3.—J. E., a 2 day old boy, was born at home. The labor was uncomplicated. Shortly after birth the child began vomiting whenever fluid was given by mouth. Emesis was projectile, and the vomitus was greenish. On the second day breast feedings were given, but the emesis continued. The child passed a small number of green meconium stools. There had been no fever, and the infant appeared active.

When examined on the second day of life, April 13, 1938, the child was only moderately dehydrated and did not appear ill. The anterior fontanel was not sunken. The abdomen was slightly distended. The liver and spleen were not palpable. The umbilical cord was attached and did not appear infected.

Fig. 10 (case 3).—Roentgenogram obtained after a barium sulfate enema. The large filling defect caused by the intramural cyst is seen in the ileocecal region.

The urine was normal, and the Wassermann and Kahn reactions were negative. The hemoglobin content was 104 per cent, the red blood cells numbered 5,100,000 per cubic millimeter, the white blood cells numbered 7,200, and the differential count was normal.

Fluids were given subcutaneously and intravenously shortly after the patient's admission. Water was given by mouth, but this was vomited. On the day following admission the child's temperature rose to 39.2 C. (102.6 F.), and the abdomen appeared more distended.

Roentgen examination of the abdomen showed a large amount of gas in the small intestines. This was not believed, however, to indicate definite intestinal obstruction. On the following day the child's gastrointestinal tract was examined further by the use of barium sulfate. Dr. Miller, of the department of roentgenology, gave the following report:

Many loops of gas-filled bowel were seen. The enema easily filled the colon up to the middle of the ascending portion. At this point there was slight delay of filling. As the enema pressure increased, the cecum filled, and there was slight spilling into the ileum. The colon from the middle of the ascending colon distally appeared normal. The cecum was not well filled. There appeared to be an intraluminal defect (fig. 10). The appearance was highly suggestive of intussusception, but since intussusception is extremely rare in a child of this age, the more likely possibility was believed to be a congenital cyst or some other intraluminal lesion in the cecum.

An exploratory laparotomy was performed on April 15 by Dr. H. P. Jenkins, of the department of surgery. The small intestine was markedly distended. The terminal part of the ileum contained a mass, which caused considerable swelling of the bowel at that point. The cecum was collapsed, as was also the ascending colon. The ascending colon was mobilized, and a lateral anastomosis was made between the terminal part of the ileum above the mass and the ascending colon.

The child had a rather stormy postoperative course for the first three days. Fluids were given parenterally, and a constant suction apparatus was used for lavage of the stomach. Repeated blood transfusions were used to restore serum proteins. On April 18, the third postoperative day, the temperature dropped to normal, and the gastric aspiration was discontinued. The child's subsequent postoperative course was uneventful. He began to take breast milk on the third postoperative day and retained most of his feedings. He gained weight during his hospital stay and was discharged entirely well on May 20, thirty-six days after admission. Roentgen examination on the day before discharge showed that the entire colostomy was functioning adequately.

The boy was seen in the outpatient department when 3 months of age. At that time he weighed almost 12 pounds (5,443 Gm.); he had gained 2 pounds and 11 ounces (1,219 Gm.) since his discharge, seven weeks previously. Bowel movements had been normal, and no vomiting had occurred.

COMMENT

Intramural enterogenous cysts occur more often in the ileocecal region than in any other portion of the intestinal tract. Tables 1 and 2 were compiled from a review of reported cases. The rarity of enterogenous cysts in the duodenal region is of interest, since only 8 cases have hitherto been reported; in 7 of these the cysts were intramural. The cysts may lie within any of the layers of the intestinal wall, on the mesenteric or the antimesenteric side, and are usually described as subserous, intermuscular or submucosal, depending on the region within which they are found (fig. 11). The intermuscular location is apparently the most common (table 3).

The ages of the patients whose cysts have been described vary from newborn to 62 years. The age depends to a large extent on the region in which the cyst is located, the size of the tumor and the presence of complications, such as intussusception. All of the duodenal cysts, with the exception of that of the 14 year old girl described by Gardner and Hart, have been found in infants under the age of 4 months. Cysts occurring in the ileocecal region are less likely to be found early in life, unless the size or location causes symptoms and signs necessitating a surgical procedure.

Author	Sex and Age of Patient	Location of Cyst	Symptoms	Physical Signs	Preoperative Diagnosis and Operative Procedure	Comment
Roth [1a]	Male, newborn	(1) Cyst of third portion of duodenum; (2) Cysts also in thorax and at end of Meckel's diverticulum	.....	Abdomen greatly distended	No operative procedure	Child died 10 min. after birth
Meyer [2b]	Female, 3 wk.	In duodenal wall between pylorus and duodenum (intermuscular)	Persistent vomiting beginning at 2 wk.; loss of weight	Emaciation and dehydration; generalized anasarca	Diagnosis: pylorospasm; no operative precedure	Child died 30 days after admission to hospital
Waugh [2c]	Female, 19 days	Posterior wall of second portion of duodenum	Regurgitation of breast milk shortly after birth; this increased and child then began vomiting projectally; cried continuously, lost weight and was constipated	Distention of abdomen and prominence in right upper quadrant; firm rounded mass palpated in right side of abdomen	Preoperative diagnosis questionable; operative procedure: cyst wall incised and cyst evacuated, then packed; packing removed and tube inserted into cyst cavity; recurrence of symptoms 6 wk. later; cyst evacuated again, wall sutured to aponeurosis of abdominal wall and tube inserted into cavity	Child died 6 days after second operation (bronchopneumonia)
Maddox [2d]	Sex not stated, 3 mo.	In entire second portion of duodenum (intermuscular)	Projectile vomiting after feedings, beginning at 6 wk.	Emaciation and anemia; peristaltic waves visible; large hard nontender mass palpable in right upper quadrant; results of rectal examination negative	Preoperative diagnosis questionable; pyloric obstruction, cause unknown; operative procedure: child's condition too poor for posterior gastroenterostomy	Child died 16 hr. after admission
Smith [2e]	Female, 2 wk.	Anterior wall of first portion of duodenum	Infant breast fed; vomited after almost every feeding, sometimes projectally	Distention of abdomen; visible peristalsis seen occasionally in epigastrium; indefinite tumor palpated in right costal margin; barium sulfate studies showed no obstruction	Preoperative diagnosis: congenital pyloric stenosis; operative procedure: section of cyst wall excised; stomach opened and dilators passed through pylorus into duodenum; stomach closed and cyst drained	Child died 7 days after operation
Gardner and Hart [2f]	Female, 15 yr.	Upper third of duodenal wall	Unexplained hematemesis and melena at 6 mo. and at 2 yr.; vague abdominal pains starting at 3 yr.; hematuria on one occasion; appendectomy at 2 yr.; emesis with attacks of pain at 13 yr.; bile in vomitus; mass appeared in right upper quadrant	Visible fulness in right upper quadrant; indenite tender mass in region of gallbladder; mass was smooth and did not descend with respiration	Preoperative diagnosis questionable; operative procedure: anastomosis of cyst cavity with duodenal lumen, made by making opening into cyst through duodenal wall	Patient completely recovered
Basman [2g]	Female, 4 wk.	Upper half of first portion of duodenum (anterior wall)	Began vomiting projectally at 11 days; vomitus did not contain bile; stools normal; loss of weight	Dehydration and malnourishment; no peristaltic waves visible; freely movable tumor mass palpated in abdomen	Preoperative diagnosis: pyloric stenosis; operative precedure: aspiration of cyst followed 7 days later by gastroenterostomy	Child recovered
Pachman (case 1)	Female, 4 mo.	First portion of duodenum (intermuscular)	Inconstant swelling noted in right side of abdomen at 3 mo.; occasional vomiting; persistent vomiting associated with otitis media at 4 mo.	Freely movable mass palpated in right side of abdomen; peristaltic waves visible; results of barium sulfate studies negative	Preoperative diagnosis: cyst of abdomen; operative procedure: small section of cyst wall removed and catheter inserted (partial marsupialization)	Child died 4 hr. after operation

TABLE 2.—*Enterogenous Intramural*

Author	Sex and Age of Patient	Location of Cyst	Symptoms
Fraenkel, E.: Virchows Arch. f. path. Anat. **87**: 275, 1882 (Gaedechen's case, 1851)	Female, 11 days	At ileocecal valve near mesenteric insertion (intermuscular)	Constipation; fecal vomiting began on third day
Dittrich, P.: Ztschr. f. Heilk. **6**: 277, 1885	Female, 12 days	In lower end of ileum (intermuscular)	.....
Sainsbury, H.: Tr. Path. Soc. London **38**: 146, 1886	Female, 11 yr.	Anterior wall of cecum near ileocecal valve	.....
Dittrich, P.: Prag. med. Wchnschr. **14**: 307, 1889	Female, 5 yr.	In lower end of ileum (intermuscular)	.....
Seeligmann, G.: Jahrb. d. Hamb. Staatskrankenanst. (1890) **2**: 129, 1892	Male, 1 yr. 9 mo.	In lower end of ileum (intermuscular)	.....
Heuter, C.: Beitr. z. path. Anat. u. z. allg. Path. **19**: 341, 1896	Infant	Intramural cyst at ileocecal valve (submucous)	.....
Quensel, U.: Nord. med. Ark. (pt. 6, no. 30) **9**: 1, 1898	Infant	Antimesenteric wall of ileum near cecum (submucous)	.....
Quensel, U.: Nord. med. Ark. (pt. 6, no. 30) **9**: 1, 1898	Female, 4 mo.	Antimesenteric wall of ileum near cecum (submucous)	.....
Quensel, U.: Nord. med. Ark. (pt. 6, no. 30) **9**: 1, 1898	Female, 62 yr.	Antimesenteric wall of lower part of ileum (intermuscular)	Abdominal pain, constipation and fecal vomiting
Quensel, U.: Nord. med. Ark. (pt. 6, no. 30) **9**: 1, 1898	Adult (sex and age not given)	Antimesenteric side of ileum (subserous)	.....
Sprengel: Arch. f. klin. Chir. **61**: 1032, 1900	Female, 15 yr.	Intramural cyst at ileocecal valve (intermuscular)	Periodic attacks of abdominal pain accompanied by vomiting since the age of 4 yr.; last attack shortly before admission to hospital
Gfeller, L.: Deutsche Ztschr. f. Chir. **65**: 330, 1902	Female, 11 yr.	In lower end of ileum (intermuscular)	Periodic attacks of abdominal pain and vomiting for 7 yr.
Krogius, A.: Ztschr. f. klin. Med. **49**: 53, 1903	Female, 2 mo.	At angle between ileum and cecum (intermuscular)	Constipation noted at 6 wk., followed shortly by fecal vomiting
Ayer, J. C.: Am. J. M. Sc. **131**: 89, 1906	Male	Intramural mass at ileocecal junction	Intermittent attacks of constipation, fever and vomiting for 7 yr.
Neupert: Zentralbl. f. Chir. **37**: 714, 1910	Male, 10 yr.	Antimesenteric side of lower end of ileum (intermuscular)	Painful swelling in ileocecal region
Blackadar, A. D.: Tr. Am. Pediat. Soc. **25**: 296, 1913	Male, 10 wk.	In wall of cecum opposite ileocecal valve	Vomiting for 2 wk.
Ball, A. G.: Brit. J. Child. Dis. **11**: 259, 1914	Male, 3 mo.	Posterior wall of cecum	Short history of 48 hr., severe pain and symptoms of acute intestinal obstruction

Physical Signs	Preoperative Diagnosis and Operative Procedure	Comment
Signs of acute intestinal obstruction	No clinical impression given; no operative procedure	Child died
.....	.....	Child died of pneumonia; cyst was incidentally observed at autopsy
.....	.....	Child died of typhoid fever
.....	.....	Child died of diphtheria; no clinical symptoms or physical signs caused by cyst during life
.....	.....	Child died of pneumonia; no clinical symptoms or physical signs caused by cyst during life
.....	.....	Cyst noted at autopsy; no clinical symptoms or physical signs caused by cyst during life
.....	.....	Cyst noted at autopsy
.....	.....	Child died of pneumonia; cyst noted at autopsy; no clinical or physical signs caused by cyst reported
Signs of acute intestinal obstruction	Preoperative diagnosis questionable; operative procedure: laparotomy with resection of pelvic tumor and adhering parts of the intestine; torsion of the cyst present	Patient died
.....	.....	Specimen obtained from Stockholm Pathologic Institute; tuberculous ulcers noted in small intestine and in cyst wall
Abdomen tense; transverse tumor palpated in supraumbilical region	Preoperative diagnosis: tuberculous peritonitis; operative procedure: intussusception of intestine containing cyst into ascending colon found; resection of part of colon and ileum containing tumor performed	Patient recovered
Abdomen distended; diffuse abdominal tenderness on pressure	Preoperative diagnosis: peritonitis following rupture of appendix; operative procedure; enucleation of cyst; peritoneum and longitudinal muscle fibers divided and tumor mass shelled out	Child recovered
Paleness and emaciation; large tense distended abdomen; peristaltic waves visible; no tumor palpable	Preoperative diagnosis: intestinal obstruction, cause unknown; operative procedure: ileostomy, followed 4 days later by resection of tumor with neighboring parts of ileum and cecum	Child died 2 hr. after last operative procedure
Slight tenderness and resistance at McBurney's point; no masses felt	Preoperative diagnosis: catarrhal appendicitis; operative procedure: free portion of cyst wall trimmed off within ½ inch (1.3 cm.) of its point of fusion with intestine and wound in intestine sutured; cigaret drain left	Patient recovered; drain removed on 3d day; excised portion of cyst wall lost and hence not examined
Mass palpable in ileocecal region; pain in that region on pressure	Preoperative diagnosis questionable; operative procedure: resection of lower part of ileum and ascending colon	Child recovered
Abdomen distended; peristaltic waves visible; sausage-shaped tumor palpated in right lower quadrant	Preoperative diagnosis: ileocecal intussusception; operative procedure: resection of cyst, cecum and appendix and end to end anastomosis	Child recovered
Abdomen distended and rigidity present; mass palpated in right iliac fossa; no mass felt in rectum	Preoperative diagnosis: intussusception causing partial intestinal obstruction; operative procedure: resection of part of ileum, cecum, cyst and small portion of ascending colon; lateral anastomosis; fecal fistula developed, and 6 months later child also had another attack of acute intestinal obstruction, caused by a band of fibrous tissue; obstruction relieved and fistula closed	Child recovered

TABLE 2.—*Enterogenous Intramural Cysts*

Author	Sex and Age of Patient	Location of Cyst	Symptoms
Lotheissen, G.: Deutsche Ztschr. f. Chir. **179**: 394, 1923	Female, 21 yr.	Cecal cyst (intermuscular)	Sharp pains in right lower quadrant
MacCauley, H. F.: Brit. J. Surg. **11**: 122, 1923	Female, 6 mo.	Intramural cyst at ileocecal angle	Sudden abdominal pain and vomiting; had attack of severe colic at 6 wk.
Bazin, A. T.: Canad. M. A. J. **15**: 130, 1925	Male, 8 mo.	Medial wall of cecum just above ileocecal valve (intermuscular)	Colic, vomiting, constipation and fever for 5 days
Edwards, H., 1928, cited by Evans	Female, 12 yr.	Right wall of cecum just below ileocecal valve	Symptoms of acute appendicitis
Beekman, F.: Ann. Surg. **90**: 1097, 1929	Female, 5½ yr.	Intramural cyst in medial wall of cecum just proximal to ileocecal valve	24 hr. before admission, sudden onset of cramplike pains in right lower quadrant, followed by vomiting; no mucus or blood passed by rectum
Evans, A.: Brit. J. Surg. **17**: 34, 1929	Male, 29 yr.	Intramural cyst of cecum (intermuscular)	2 year history of intermittent griping pains in lower part of abdomen; anorexia and malaise
Drennen, E.: Arch. Surg. **22**: 106, 1931 (case 1)	Sex not recorded, 9 mo.	Intramural cyst of ileum arising just above ileocecal valve (intermuscular)	Symptoms of acute intestinal obstruction
Drennen, E.: Arch. Surg. **22**: 106, 1931 (case 2)	Sex not recorded, 2 yr.	In ileum just above ileocecal valve (intermuscular)	Vomiting and bloody stools of 6 days' duration
Drennen, E.: Arch. Surg. **22**: 106, 1931 (case 3)	Female, 21 yr.	Cecal cyst (submucous)	Pain over cecal region
Pachman (case 2).....	Male, 8 mo.	Lower part of ileum (intermuscular)	Abdominal pain, vomiting and constipation
Pachman (case 3).....	Male, 2 days	Within wall of terminal part of ileum	Vomiting of bile-stained material shortly after birth; small number of meconium stools

Except in 2 cases (in 1 of these the sex was not given), all the patients with duodenal cysts were females. Cysts in the ileocecal region also occurred more frequently in females than they did in males (table 4).

The symptoms vary with the location of the cysts. In many cases, taking of a careful history would reveal that on previous occasions

of the Ileocecal Region—Continued

Physical Signs	Preoperative Diagnosis and Operative Procedure	Comment
Tumor palpable in right lower quadrant	Preoperative diagnosis questionable; operative procedure: resection of cyst and cecum	Patient recovered
Child in excellent health; signs of acute intussusception present; tumor palpable along course of descending colon	Preoperative diagnosis: acute intussusception; operative procedure: intussusception present but cyst was also found; resection of part of bowel containing tumor and side to side anastomosis	Child died 6 hr. after operation
Physical examination with child under anesthesia; abdomen distended, mass palpable on left side; digital examination revealed indefinite fulness in upper portion of pelvic brim	Preoperative diagnosis: intussusception; operative procedure: intussusception found secondary to cyst; resection of cecum, cyst and part of ileum and lateral anastomosis	Child recovered
Signs of acute appendicitis; variable tumor in cecal region also felt	Preoperative diagnosis questionable; operative procedure: resection of tumor mass	Child recovered
Abdomen soft, no tenderness present; active peristalsis visible; freely movable sausage-shaped mass felt in right lower quadrant	Preoperative diagnosis: partial intestinal obstruction, probably due to intussusception; operative procedure: enucleation attempted, but cyst ruptured; marsupialization of cyst then done; fecal fistula resulted when small hole in cyst occurred; 7 months later fistula and opening into intestine closed	Child recovered
Patient had noted an inconstant mass in right lower quadrant for 1 yr.; tumor palpable (inconstant) in line of ascending colon at admission	Preoperative diagnosis questionable; operative procedure: enucleation unsuccessfully attempted; cecum and adjoining ileum excised; anastomosis made between end of ileum and side of ascending colon	Patient recovered
Movable nontender tumor mass in region of cecum	Preoperative diagnosis: acute intestinal obstruction, cause unknown; operative procedure: resection of 2 in. (5 cm.) of terminal ileum together with cecum and appendix and 3 in. (7.6 cm.) of ascending colon; side to side anastomosis then made	Child recovered
Tenderness and rigidity over McBurney's point	Preoperative diagnosis: questionable intussusception; operative procedure: intussusception found which could not be reduced, as ileum had sloughed; all of intestine which contained intussuscepted parts excised and ileum joined to sigmoid by lateral anastomosis	Child died 1 hr. after operation
Tenderness and rigidity	Preoperative diagnosis questionable; operative procedure: caput cecum, cyst and appendix excised and defect repaired by suture	Patient recovered
Sausage-shaped mass palpable in transverse position above umbilicus; results of rectal examination negative	Preoperative diagnosis: intussusception; operative procedure: intussusception secondary to cyst within wall of ileum found; cyst, ileum, cecum and a portion of the ascending colon resected and lateral anastomosis made between proximal ileum and transverse colon; intussusception recurred 12 days after discharge but was reduced successfully	Child ultimately recovered
Moderate dehydration; abdomen distended; no masses palpable	Preoperative diagnosis: acute intestinal obstruction, possibly due to intramural cyst; operative procedure: ascending colon mobilized and lateral anastomosis made between terminal ileum above tumorous mass and ascending colon	Child recovered

the patient has had vague gastrointestinal complaints, which were probably caused by the tumor mass. Duodenal cysts simulate pyloric stenosis most frequently. Vomiting, which is usually projectile, may start at birth or a short time later and usually becomes persistent. The chief complaint may be, as in case 1, a tumor mass which has not as yet caused symptoms.

Ileocecal intramural cysts may cause abdominal pain, distention, vomiting, diarrhea or constipation. When intussusception secondary to such a cyst occurs, the symptoms of that condition are present. In this series, intussusception was found in 6 cases.

A freely movable tumor mass has been the outstanding physical sign. The size of the mass, however, varied considerably in the different patients and in some cases also changed in the same patient. In the cases of duodenal cyst the mass is usually described as a "rather large pyloric tumor." In case 1 the size of the tumor made the diagnosis of pyloric stenosis unlikely. Ileocecal cysts are seldom palpable unless they reach considerable size. Abdominal distention often makes

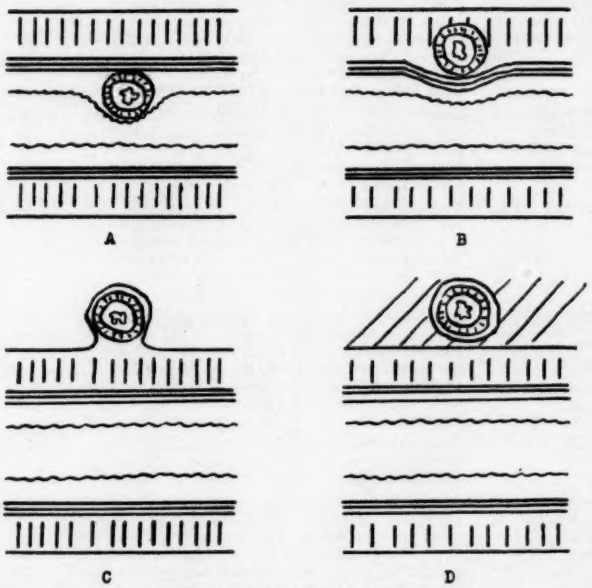

Fig. 11.—The various positions in which abdominal enterogenous cysts may be found: *A,* submucosal; *B,* intermuscular; *C,* subserous, and *D,* intramesenteric. The vertical lines represent the longitudinal muscular coat; the triple horizontal lines, the circular muscular coat, and the wavy lines, the mucosa (modification of an illustration in Evans, A.: Developmental Enterogenous Cysts and Diverticula, Brit. J. Surg. **17**:34, 1929).

palpation of such a tumor difficult. If intussusception occurs as a result of a cyst of this type, the sausage-shaped mass characteristic of that condition may be found. Peristaltic waves may be seen, particularly with obstruction in the duodenal region. In cases of cyst of the ileocecal region, digital examination of the rectal region often reveals the presence of the tumor.

The correct diagnosis is usually made only at operation or at post-mortem examination. Histologic examination of a section of the cyst

wall reveals the true nature of the mass. Nevertheless, an abdominal cyst should be suspected when a freely movable, variable, soft mass can be palpated. If vomiting and abdominal pain also occur, the likelihood that the mass is a cyst is increased. If no symptoms of obstruction are present, an intravenous pyelogram may eliminate the possibility of a renal tumor. Digital examination by rectum may reveal a cystic mass in the pelvic brim.

Roentgen examination of the gastrointestinal tract may or may not be an aid in diagnosis. It is noteworthy that in case 1, despite the huge size of the cyst, there was no obstruction to the passage of barium sulfate. Yet this child was having definite signs of obstruction (peristaltic waves, vomiting) at that time. However, in case 3 the possibility of an

TABLE 3.—*Location of Intestinal Cysts*

Section of Intestine	Total Number of Cases	Layer of Intestine			
		Subserous	Intermuscular	Submucous	Unknown
Duodenum	8	0	3	0	5
Ileum	13	1	9	2	1
Ileocecal junction	6	0	3	1	2
Cecum	9	0	3	1	5
Total	36	1	18	4	13

TABLE 4.—*Distribution of the Cysts According to Sex*

Location	Female	Male	Sex Not Recorded
Duodenum	6	1	1
Ileocecal region	14	9	5
Total	20	10	6

enterocystoma was suggested by Dr. J. F. Miller, of the department of roentgenology, when an intraluminal filling defect was noted.

If intussusception occurs because of a cyst, the true cause of the condition may be entirely masked and may be revealed only at the time of operation.

Hypertrophic pyloric stenosis is the condition usually suspected before operation when a cyst is located in the duodenal region. When the cyst is found in the ileocecal region the most frequent preoperative diagnoses are intestinal obstruction caused by intussusception or by an unknown factor, appendicitis and tuberculous peritonitis.

Various surgical procedures have been used in the treatment of intramural cysts. The enucleation of such a tumor is both difficult and dangerous, owing to its intimate relation with the intestinal wall. Although this procedure is particularly successful when a cyst is within

the mesentery, it can be used only in well selected cases of intramural cyst, in which the danger of perforation of the intestine is minimal.

Treatment of the cysts by marsupialization has been advocated. By this procedure a cyst is opened, its edges are sutured to an opening in the peritoneum and the cyst is then drained by means of a catheter.

The portion of the intestine which contained the tumor mass has been resected, particularly when the cyst involved the ileocecal region. When the cyst has caused intussusception, the resection of both the intussusception and the intussuscipiens may be necessary.

TABLE 5.—*Mortality in Cases of Intramural Duodenal and Ileocecal Cysts*

Location	Recovery	Percentage of Corrected Recovery	Death	Percentage of Corrected Mortality	Death Due to Cause Other Than Cyst
Duodenum	2 (25%)	28.5	5 (62.5%)	71.5	1 (12.5%)
Ileocecal region	15 (53.5%)	75	5 (18%)	25	8 (28.5%)
Total	17 (47.2%)	63	10 (27.8%)	37	9 (25%)

TABLE 6.—*Operative Procedures Reported in this Series of Cases*

Operative Procedure	Ileocecal Region			Duodenal Region		
	No. of Cases	Recovery	Death	No. of Cases	Recovery	Death
Resection	15	11 (73.3%)	4 (26.7%)	..	..	..
Marsupialization	2	2 (100%)	..	3	0	3 (100%)
Enucleation (no other procedure used)	1	1 (100%)	..	..	..	..
Gastroenterostomy or enterocolostomy (cyst wall left intact)	1	1 (100%)	..	1	1 (100%)	..
Anastomosis of cyst cavity with intestinal lumen	..	..	..	1	1 (100%)	..

The cyst has been evacuated by making an anastomosis between its cavity and the intestinal lumen. Gardner and Hart [2f] stated the belief that this is the method of choice for an intramural duodenal cyst, which cannot be excised. Infection of the cavity of the tumor may occur, however, as a result of the spilling of intestinal contents into it.

A procedure has been performed in which the cyst wall is left intact and an entero-enterostomy is made above the obstructing mass. When this method is used there is always a possibility that the cyst will subsequently become larger and thus cause pressure symptoms.

In this series only 2 recoveries followed operative procedures on the duodenal cysts (tables 5 and 6). In one of these, the procedure advocated by Gardner and Hart [2f] was used, while in the other, reported

by Basman,[28] a gastroenterostomy was performed. Three of the fatalities followed attempts at drainage through marsupialization of the cysts. There is no doubt that the age of this group was partly responsible for the high mortality.

Cysts in the ileocecal region, however, offer a more favorable prognosis, 75 per cent of the patients having recovered (table 5). Resection of the portion of intestine containing the cyst was the operative procedure most frequently used (table 6). The low mortality with this method is surprising, not only because of the magnitude of the operation but because in a number of cases it was used only after other methods had failed. The presence of intussusception also added to the operative risk in many of these cases. Marsupialization of the cyst was used for 2 patients with an ileocecal cyst, both of whom recovered. Enucleation alone was performed successfully in 1 case, but in other cases this procedure was attempted and later abandoned, as too hazardous, in favor of resection. An enterocolostomy, without removal of the cyst, was performed for 1 patient (case 3), and the child made a complete recovery.

The postoperative care, particularly of young infants, is extremely important. Fluids are given parenterally during the first few days. Transfusions are usually necessary to restore depleted proteins and to combat anemia, especially if large amounts of fluids have been given parenterally. In both case 2 and case 3 continuous gastric lavage was used. This procedure contributed considerably to the favorable course of these patients.

SUMMARY

Three cases of intramural enterogenous cyst of the intestine are reported.

Thirty-three similar cases gathered from the literature are tabulated.

The symptoms and physical signs caused by intramural enterogenous cysts are discussed.

These cysts occur most frequently in females and more often in the intermuscular layer of the ileocecal region than in any other position.

The various types of operations used are briefly discussed, and the operative mortality is tabulated.

NEW CREATININE STANDARD FOR BASAL METABOLISM AND ITS CLINICAL APPLICATION

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I. NORMAL CHILDREN: GROUP A

The study reported in this section of the present paper extended and confirmed previous investigations on the relation between creatinine excretion and basal energy metabolism.[1] In a recent publication [1b] two of us with F. Broughton presented a creatinine standard of metabolism which was based on a mixed group composed of "hospital normal" patients, normal children and normal adults. Those studies were carried further with the series of subjects reported on here. This group was made up entirely of normal school children and may therefore be considered ideal. Using the newer series alone, we prepared a new creatinine standard by statistical methods.

The data were obtained from two groups of children who differed in age and socioeconomic status. The children composing the first group attended a private day school. They were enrolled in a growth study project,[2] the physical aspects of which were being carried out under the direction of the Department of Child Hygiene, Harvard School of Public Health, under a grant from the Board of General Education. In this connection, 30 observations were made on 16 boys

From the Department of Pediatrics of the Harvard Medical School, the Departments of Child Hygiene and of Vital Statistics of the Harvard School of Public Health, the Infants' Hospital and the Children's Hospital.

1. (*a*) Talbot, N. B.: Basal Energy Metabolism and Creatinine in the Urine: I. Observations on Children, Am. J. Dis. Child. **52**:16 (July) 1936. (*b*) Talbot, N. B.; Stewart, A. H., and Broughton, F.: Basal Energy Metabolism and Creatinine in the Urine: II. Prediction of Basal Heat Production from Creatinine, ibid. **56**:965 (Nov.) 1938.

2. Other members of the research group and the school staff gave assistance in obtaining the cooperation of the children, and Miss Frances Broughton and Miss Penelope Hill gave technical assistance.

(1 M) ranging in age from 7 to 14 years inclusive, and 51 observations were made on 22 girls (1 F) between the ages of 6 and 14 inclusive. The second group of children were enrolled in another growth study project being conducted by the Department of Child Hygiene, Harvard School of Public Health, at a special center in Boston.[3] This project was also made possible by a grant from the Board of General Education. Sixteen observations were obtained on 14 boys from this center who were either 5 or 6 years of age (2 M). Some of these children were attending public schools in Boston. Girls enrolled at this center were also studied, but the observations made on them have been discarded because of the impossibility of securing accurate collections of urine. We believe that it is difficult to obtain complete specimens of urine from girls below 6 years of age because they tend to lose urine with the stool.

TABLE 1—*Data on Normal School Children (Group A)* *

Group	1 M	1 F	2 M
Sex	Boys	Girls	Boys
Number	30	51	14
Age range (inclusive), yr.	7-14	6-14	5-6
Average caloric output	1,435	1,231	1,002
Standard deviation of caloric output	268	181	111
Coefficient of variation of caloric output, percentage	19	15	11
Average creatinine output, mg.	932	749	391
Standard deviation of creatinine output, mg.	311	233	99
Coefficient of variation of creatinine output, percentage	33	31	25
Average weight, Kg.	41.6	38.6	20.7
Standard deviation of weight, Kg.	9.9	11.3	3.4
Coefficient of variation of weight, percentage	24	29	16
Correlation between caloric and creatinine output	0.778	0.831	0.736
Correlation between caloric output and weight	0.721	0.845	0.921

* The statistical constants given in this table may be described as follows: The standard deviation is a measure of variation about the average. Ordinarily the average plus or minus the standard deviation includes about two thirds of the observations. The coefficient of variation measures the variability relative to the average and is defined as the standard deviation divided by the average. Notice in the table that the standard deviations of creatinine for the boys, 1 M, and girls, 1 F, are 311 and 233 mg., respectively, whereas the coefficients of variation are the same, namely, 33 and 31 per cent. The correlation coefficient is a measure of the relation between two variables. A value of −1 indicates perfect negative relationship (a = −b); a value of 0, no relationship at all, and a value of +1 perfect relationship (a = b).

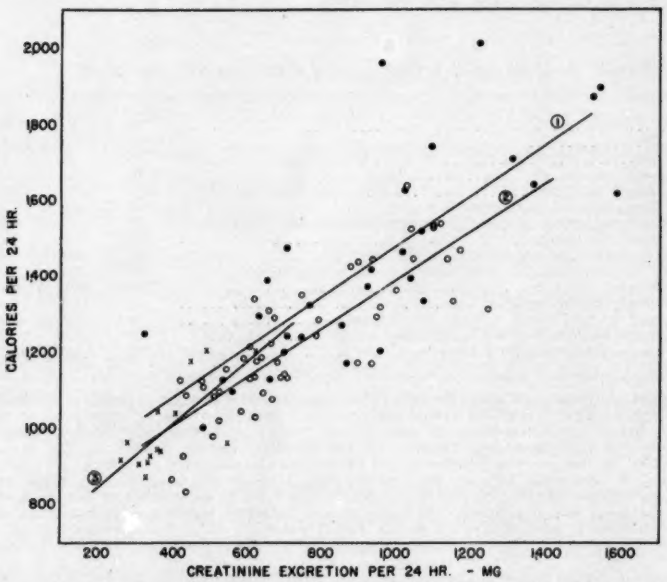
A summary of the results of the studies carried out on groups 1 M, 1 F and 2 M is given in table 1.[4] The table shows that the correlation between total basal caloric output and creatinine excretion is as good

3. The studies being conducted under this project have been fully described in a monograph accepted for early publication (Stuart, H. C., and others: The Center, the Group Under Observation; Sources of Information and Studies in Progress, Monograph of the Society for Research in Child Development, National Research Council, 1939, series 20, vol. 4, no. 1).

4. The urinary output for a day was carefully collected, and the preformed creatinine content was determined by Folin's method (Folin, O.: Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 159). The heat production was measured by the Benedict-Roth apparatus under basal conditions. All the subjects were normal healthy school children. In any case in which the determination of either creatinine excretion or caloric output was suspected to be inaccurate, both measurements were discarded.

as that between caloric output and weight.[5] The three trend lines express average normal caloric output in terms of creatinine excretion, as follows:

Line	Group	Equation
1	1 M	Caloric output = 0.669 creatinine excretion + 811
2	1 F	Caloric output = 0.645 creatinine excretion + 748
3	2 M	Caloric output = 0.825 creatinine excretion + 680



Total caloric output plotted against creatinine excretion per twenty-four hours. The dots represent the boys (1 M); the circles, the girls (1 F) and the crosses, the younger boys (2 M). Line 1 indicates the trend for group 1 M, line 2 that for 1 F and line 3 that for 2 M.

These lines [6] are shown graphically in the chart. The data for groups 1 M and 1 F have been combined to give trend coefficients and the following equations:

For the boys, caloric output = 0.657 creatinine excretion + 822.

5. Talbot, F. B.; Wilson, E. B., and Worcester, J.: Basal Metabolism of Girls: Physiologic Background and Application of Standards, Am. J. Dis. Child. **53**:273 (Jan., pt. 2) 1937.

6. Data on group 2 M are included in the chart because they suggest that the line has started to curve downward.

For the girls, caloric output = 0.657 creatinine excretion + 739. Values derived from these equations have been tabulated as a creatinine standard for metabolism in table 2.

Clinically, the height and weight standards of metabolism give accurate information about children of normal physique [7] and about many who are not of normal physique. With some children of unusual body build, however, interpretation is difficult because the percentage of musculature per kilogram of body weight varies considerably from the normal.[8] With these children metabolic rates based on the weight standard cannot be expected to reflect the activity of the heat-producing tissues (chiefly muscle). Because creatinine is a measure of muscle weight, the creatinine standard should eliminate the possibility of errors due to abnormalities of body build. This standard is therefore published here with the hope that it will make interpretations of metabolic findings more accurate.

TABLE 2.—*Standard Total Caloric Output for Creatinine Output of Boys and Girls*

Creatinine Output per 24 Hr., Mg.	Total Caloric Output per 24 Hr.		Creatinine Output per 24 Hr., Mg.	Total Caloric Output per 24 Hr.	
	Boys	Girls		Boys	Girls
350	1,052	969	850	1,381	1,298
400	1,085	1,002	900	1,414	1,331
450	1,118	1,035	950	1,446	1,363
500	1,151	1,068	1,000	1,479	1,396
550	1,184	1,101	1,050	1,512	1,429
600	1,216	1,133	1,100	1,545	1,462
650	1,249	1,166	1,150	1,578	1,495
700	1,282	1,199	1,200	1,611	1,528
750	1,315	1,232	1,250	1,644	1,561
800	1,348	1,265			

II. ABNORMAL CHILDREN: GROUP B

If the creatinine standard is to have clinical significance, it is important that the creatinine output should be constant with relation to muscle mass and independent of the total calories produced by the muscles. To test this point and to confirm the work of other investigators [9] in the field we measured the creatinine output of a small group

7. Talbot, F. B.: Basal Metabolism Standards for Children, Am. J. Dis. Child. **55**:455 (March) 1938. Talbot, Wilson and Worcester.[5]

8. Talbot, N. B., and Broughton, F.: The Measurement of Obesity by the Creatinine Coefficient, Am. J. Dis. Child. **55**:42 (Jan.) 1938.

9. Thorn, G. W.: Creatine Studies in Thyroid Disorders, Endocrinology **20**: 628, 1936. Pugsley, L. I.; Anderson, E. M., and Collip, J. B.: The Effect of Thyreotropic Hormone and of Desiccated Thyroid upon Creatine and Creatinine Excretion, Biochem. J. **28**:1135, 1934. Poncher, H. G.; Visscher, M. B., and Woodward, H.: Creatine Metabolism in Children with Hypothyroidism, J. A. M. A. **102**:1132 (April 7) 1934. Kepler, E. J., and Boothby, W. M.: Creatinuria in Hyperthyroidism, Am. J. M. Sc. **182**:476, 1931. Talbot and Broughton.[8]

TABLE 3.—*Observations on Children with Thyroid Disease (Group B)*

Patient	Age, Yr.	Height, Cm.	Weight, Kg.	Average Total Caloric Output		Increase in Total Caloric Output, Percentage	Average Creatinine Output, Mg. per 24 Hr.		Change in Creatinine Output, Percentage	Basal Metabolic Rate*				Medication
				Before Treatment	After Treatment		Before Treatment	After Treatment		Weight Standard, Percentage		Creatinine Standard, Percentage		
										Before Treatment	After Treatment	Before Treatment	After Treatment	
HYPOTHYROIDISM														
B. A. G.	4 2/12	96	15	435	820	+88	220	190	−13	−40	+15	−40	+14	Treated with thyroid for 4 weeks
M. D. V.	9 11/12	99	19	690	770	+12	290	290	0	−17	−7	−26	−17	Treated with thyroid for 4 weeks
A. D. V.	12 5/12	119	33	800	1,220	+52	410	420	0	−28	+9	−20	+20	Treated with thyroid for 3 weeks
R. W.	11	149	37	1,056	1,248	+18	886	886	0	−11	+5	−20	−5	Treated with thyroid for 2 weeks
M. F.	15	...	65	1,390	.....	..	1,600	...	..	−14	..	−21	..	
HYPERTHYROIDISM														
F. C.	6 10/12	129	21.4	1,230	.....	..	235	...	..	+48	..	+51	..	
E. G.	..	135	29	1,742	.....	..	487	...	..	+69	..	+68		

* The weight standard employed is that of Talbot.[5] The creatinine standard employed is that given in table 2 and in the chart of this paper except in case of B. A. G., F. C. and M. F., when the figure in a previous publication [2] is referred to.

of children with thyroid disease during the period when their disease was being corrected. These children, who composed part of group B, were patients in the wards of the Children's Hospital. Group B included 5 patients with hypothyroidism and 2 with hyperthyroidism. The data are shown in table 3. The creatinine output of 4 of the hypothyroid children was measured daily. The values were essentially constant through the period of observation for any given subject. Therefore the average values for the beginning and end of the period only are given.

Table 3 shows that the administration of thyroid caused definite elevation in the total caloric output but did not influence the creatinine excretion except in the first case. In this subject (B. A. G.) the suddenly elevated heat production (+ 88 per cent) would be expected to consume some of the muscular tissue, because presumably the food did not meet the caloric requirements. Therefore the creatinine (— 13 per cent) would be expected to fall as muscle was destroyed, provided the increased rate of metabolism did not alter the constant relation between creatinine excretion and muscle mass.

In table 3 at the right are the basal metabolic rates of the children in group B. In the cases of 2 children (R. W. and M. F.) the weight standard did not indicate the degree of hypothyroidism shown by the creatinine standard. Both children improved clinically after the administration of thyroid. This is evidence that the creatinine standard gave a truer picture of the clinical status of these children than did the weight standard. If this proves to be the case in studies of other abnormal subjects the use of the creatinine standard should explain many puzzling conditions and make more accurate definition of them possible.

The data in this paper show that the creatinine standard is as accurate as the weight standard for children who are normal and suggest that it is of greater accuracy for those who are abnormal. Since the determination of the creatinine output requires an accurate twenty-four hour collection of urine and laboratory facilities, it is possible that it will be impractical to apply this standard routinely. It is our belief, however, that accurate interpretation of abnormal conditions is facilitated by the use of the creatinine standard.

SUMMARY AND CONCLUSIONS

Previous work has been extended and the validity of creatinine output as a standard of basal metabolism has been confirmed by statistical methods. This standard is formulated here and a test application of it in a study of children with thyroid disorders is described. Thyroid therapy showed that creatinine excretion is independent of the rate of metabolism.

Dr. Alfred T. Shohl gave suggestions in the preparation of this paper and Prof. Edwin B. Wilson gave advice.

PREVENTION OF DIPHTHERIA

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In this review, three questions relating to the prevention of diphtheria will be critically discussed:

1. What is the best statistical method of checking the efficiency of active immunization against diphtheria?

2. What are the severity and the clinical typology of diphtheria which occurs in previously immunized children?

3. How may the limits of antitoxin treatment of toxic diphtheria be overcome by nonspecific preventive therapy?

STATISTICAL METHODS

Method Presenting Morbidity Curves Before and After the Introduction of Immunization.—Among the statistical methods used to check the efficiency of immunization there is one which is often applied in an uncritical fashion. It consists of obtaining local statistics on diphtheria morbidity before and after the introduction of active immunization in a given community. In order to use this method scientifically the natural trend of diphtheria morbidity in a certain area must be followed over a long period. In chart 1 diphtheria morbidity curves of four Central European cities (Budapest, Hungary, Königsberg and Düsseldorf, Germany, and Milan, Italy), and in chart 2 the curve of New York are presented; the period covered includes about sixty years, beginning in the nineteenth century and extending to 1935. Further European statistics are given in table 1. The material on New York is taken from the Weekly Bulletin of the Department of Health of the City of New York [1] and that on the whole United States from the Reports of the League of Nations Health Organisation,[2] starting in 1919.

From the Department of Pediatrics, University of Chicago. This work was aided by a grant from the Douglas Smith Foundation for Medical Research.

1. (*a*) Statistics and Reports on Diphtheria Morbidity, Weekly Bull. Dept. Health, City of New York **18**:324, 1929; (*b*) **20**:37, 1931; (*c*) **25**:10, 1936. (*d*) Statistics and Reports on Diphtheria Immunization, ibid. **18**:5, 1929; (*e*) **22**: 205, 1933; (*f*) **23**:88, 1934.

2. Annual Epidemiological Reports, Geneva, League of Nations Health Organisation, 1919-1935, nos. 8-20.

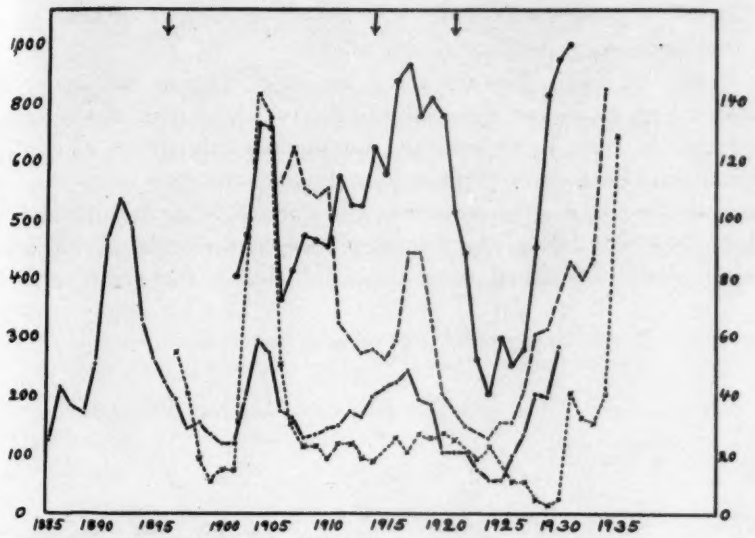

Chart 1.—Statistics of diphtheria morbidity in four European cities, showing number of cases per hundred thousand inhabitants, from 1885 to 1935. Dots and long dashes represent Budapest, Hungary; crosses and dashes, Königsberg, Germany; circles and long lashes, Düsseldorf, Germany, and dots and dashes, Milan, Italy (numbers given on right). The arrow at 1895 indicates the introduction of von Behring's antitoxin treatment of diphtheria; at 1913, the discovery by von Behring of a "new preventive against diphtheria," and at 1920, the start of large scale immunization against diphtheria in Europe.

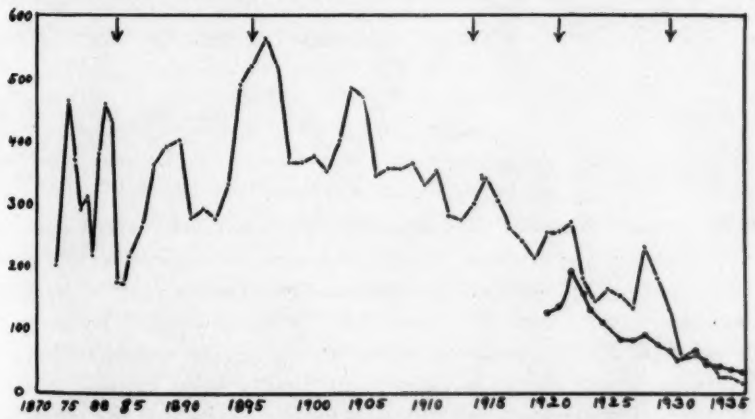

Chart 2.—Statistics of diphtheria morbidity in the city of New York (dots and dashes) and in the United States (circles and dashes), representing the number of cases per hundred thousand inhabitants from 1873 to 1935. The arrow at 1883 indicates the discovery of the diphtheria bacillus (Klebs-Löffler); at 1895 and at 1913, the events mentioned in the legend of chart 1; 1920, the start of immunization of school children against diphtheria in New York, and at 1929, the start of immunization of preschool children against diphtheria in New York.

In all of these statistics the well known century, or secular, waves of diphtheria morbidity are clearly shown.

In the European cities the waves are spectacular as they sometimes climb to high peaks and again drop to the vanishing point for a number of years. In chart 1 the peaks and low points of the curves of the four Central European cities roughly coincide as to the time of their occurrence, the peaks being encountered, with only slight deviations, in 1893, 1904, 1917 and 1930. The distances between the peaks of the waves in the seven Continental cities listed in table 1 vary from eight to

TABLE 1.—*Waves of Diphtheria Morbidity in Europe* *

City or Country	Peak	Low Point	Peak	Low Point	Peak	Low Point	Peak	Low Point	Peak	Low Point	Peak
Sweden Olin, G.: Zentralbl. f. d. ges. Kinderh. **32**: 620, 1936	1864	....	1883	....	....	....	1901	....	1919	....	....
Königsberg, Germany † Buergers [14]	....	....	....	....	....	1899	**1902**	1909	1917	1928	**1934**
Berlin, Germany † Buergers [14]	....	....	**1883**	1891	1895	1902	1911	1913	**1916**	1921	**1930**
Hamburg, Germany † Buergers [14]	....	1876	**1887**	1891	**1893**	1896	1902	1908	**1918**	1922	**1931**
Düsseldorf, Germany Hertel, J.: Veröffentl. a. d. Geb. d. Med.-Verwalt. **40**: 501, 1933	....	....	....	....	....	1901	**1903**	1905	**1916**	1923	**1930**
Cologne, Germany von Frey, W., and Thoenes, F.: Monatsschr. f. Kinderh. **49**: 33, 1931	....	....	....	....	....	....	**1910**	1913	**1918**	1926	**1930**
Budapest, Hungary Johan, B., and Tomesik, J.: Klin. Wchnschr. **9**: 1366, 1930	....	....	....	1885	**1891**	1900	**1903**	1907	1916	1923	**1929**
Milan, Italy Schwarz, W., and Fachini, G.: Arch. ital. di pediat. **3**: 259, 1935	....	....	....	....	....	....	**1906**	1914	**1917**	1923	**1933**

* High peaks in bold face figures.
† Graphs given by Buergers.

seventeen years (five and six years occurring only twice) with an average of about twelve and one-half years. The same is true of the low points of the curves. In Sweden, the distance between the peaks is eighteen to nineteen years. On the whole, there is no downward trend in the European curves of diphtheria morbidity during the period under consideration. As to the earlier history of diphtheria in Europe, e. g., in Germany, a terrifying epidemic during the second half of the eighteenth century is recorded, whereas in the first half of the nineteenth century only small sporadic epidemics occurred. Beginning about 1850, universal epidemics flared up again, the last of them being indicated in chart 1 and table 1.

In North America, in particular in the city of New York, the secular curve of diphtheria morbidity has a different shape from those of Central

Europe. The characteristic waves are present, but their amplitude is not as high as in Europe, and the incidence of diphtheria does not come to the vanishing point until recent years. The cycle of the waves averages six and one-half years, which is about half the period of the Central European cities. Furthermore, the American cycle does not at all coincide with the European cycle, as for instance in the years 1895, 1914 and 1921. Finally, there is a definite downward trend in the diphtheria morbidity curve of New York during the period from 1895 to 1935, which gradually brings diphtheria to an ever lower level in recent times (chart 2).

This is not the place for discussion of the underlying causes of the secular waves of diphtheria morbidity (Gottstein [3]). It may only be mentioned that the cycle of the waves is becoming shorter in proportion to the density of the population, the cycle being nineteen years in sparsely populated Sweden, twelve and one-half years in medium-sized Central European cities and six and one-half years in the great metropolis of New York.

The efficiency of active immunization against diphtheria, as well as any other newly introduced preventive or therapeutic measure, should be checked against the background of the secular waves of diphtheria morbidity by the statistical method under consideration. Failure to do so has led to wrong conclusions in similar cases, for example in the case of antitoxin therapy of diphtheria introduced by von Behring in 1894. Unfortunately, in most European countries and in the city of New York this historic event coincided with a spontaneous culmination or downward trend of the diphtheria morbidity curve, the credit for which was given to the antitoxin treatment (charts 1 and 2). As had been forecast by Gottstein [3b] in 1896, after the low tide of 1900 the next spontaneous wave of diphtheria morbidity came to its peak in 1904 and thereafter and sloped again to a new low point shortly before the World War. After this disappointing experience with his first discovery, von Behring,[4] in 1913, reported his "new preventive against diphtheria," which consisted of toxin-antitoxin injections. The first immunizations of children ever done were performed by von Behring's clinical collaborators, Hagemann [6] and Kleinschmidt (now at Cologne) and Viereck.[7] The first mass immunization of children against

3. Gottstein, A.: (*a*) Epidemiologische Studien über Diphtherie und Scharlach, Berlin, Julius Springer, 1895; (*b*) Berl. klin. Wchnschr. **33**:345, 1896.

4. von Behring, E.: Deutsche med. Wchnschr. **39**:873, 1913; in discussion on Hahn; [8a] Verhandl. d. deutsch. Kong. f. inn. Med. **31**:1, 1914.

5. Footnote deleted on proof.

6. Hagemann, R., cited by von Behring, E.: Gesammelte Abhandlungen, Bonn, A. Marcus and E. Weber's Verlag, 1915, pp. 57 and 75.

7. Kleinschmidt, H., and Viereck: Deutsche med. Wchnschr. **39**:1377, 1913.

TABLE 2.—*Survey of the Literature on Clinical Typology of Diphtheria of the Throat in Immunized Children* *

Place of Investigation	Author	Number of Cases	Localized Pharyngeal Diphtheria, Mild and Medium	Laryngeal Diphtheria	Toxic Diphtheria	Death from: Croup	Death from: Toxic Diphtheria
Paris, France	Discussion in Bull. Soc. de pédiat. de Paris **27**: 431, 1929	70	59	3	8	0	2
Marseille, France	Philip: Bull. Soc. de pédiat. de Paris **27**: 536, 1929	9	8	1	0	0	0
Paris, France	Mozer, G., and Mozer, M.: Presse méd. **37**: 1543, 1929	11	11	0	0	0	0
Paris, France	Lardier, J.: Angines diphtériques, Thesis, Paris, 1930 †.....1 or 2 injections	37	24	2	11	1‡	3
	3 injections	16	11	0	5	0	3
Geneva, Switzerland	Gautier, P.: Rev. méd. de la Suisse Rom. **50**: 274, 1930	3	3	0	0	0	0
Munich, Germany	Pfaundler, M.: München. med. Wchnschr. **78**: 1207, 1931	18	16	1	1	0	0
Argentina	Cibils Aguirre, R.: Zentralbl. f. d. ges. Kinderh. **28**: 517, 1934	14	14	0	0	0	0
La Basse, France	Hoffmann, A.: Bull. méd., Paris **47**: 78, 1933	24	13	0	11	0	3
Paris, France	Landau, L.: La diphtérie chez des vaccinés, Thesis, Paris, Libr. M. Lac, 1932	59	54	0	5	0	0
Turin, Italy	Lucca, A., and Fos, A.: Boll. Soc. ital. di pediat. **1**: 345, 1932	6	5	0	1	0	0
Hungary	Ormos, P.: Orvosi hetil. **75**: 861, 1931	6	6	0	0	0	0
Rome, Italy	Spolverini, L. M.: Policlinico (sez. prat.) **39**: 1949, 1932 §	10	8	2	0	0	0
Hungary	Tomcsik, J.: Deutsche med. Wchnschr. **58**: 1884, 1932	102	95	1	6	0	3
Paris, France	Fayot, M.: La diphtérie des vaccinés, Thesis, Paris, 1933 ‖.....1 or 2 injections	46	28	1	17	0	3
	3 injections	84	55	5	24	1	6
Warsaw, Poland	Kaczynski, R.: Zentralbl. f. d. ges. Kinderh. **29**: 329, 1934	47	36	0 ?	11 ?	0	0
Geneva, Switzerland	Lehmann, H.: La diphtérie chez les vaccinés, Thesis, Geneva, 1933	9	9	0	0	0	0
Russia	Sdrodowski: Arch. biol. Wissensch. **35**: 123, 1934.....1 or 2 injections	84	76 ?	0	8 ?	0	4
	3 injections	108	102 ?	0	6 ?	0	2
Saint-Etienne, France	Poulin, P.: Bull. Acad. de méd., Paris **113**: 201, 1935	71	<67	0	>4	0	4
Leeds, England	Underwood, E. A.: Lancet **1**: 364, 1935	14	13	0	1	0	0
Prague, Czechoslovakia	Prochazka, J.: Rev. d'hyg. **58**: 201, 1936	32	17	0	15	0	1
Geneva, Switzerland	Reh, T.: Presse méd. **45**: 892, 1937	17	17	0	0	0	0
		897	747	16	134	2	34

* Unless otherwise stated, three injections, usually of toxoid, were made in each case at least a few weeks previously.

† This report contains part of the cases mentioned in the 1929 Paris Discussion. In most cases in which one or two injections were made diphtheria immediately followed the last injection.

‡ Treatment on the eighth day of sickness.

§ Two cases of this series were omitted; 1 patient died of simultaneous toxic scarlet fever and 1 of severe croup only eight days after the last injection.

‖ Cases in which late palsies occurred are registered under "toxic diphtheria"; of the patients who died of the toxic type, 4 died within the first six days of illness.

diphtheria was organized by von Behring (Hahn and Sommer [8]) in 1913 near Magdeburg, Germany, and reported on by Bieber [9] in 1920. In the meantime, during the years of the World War, another big wave of severe diphtheria swept over Europe, coming to an end early in the decade 1920 to 1930. At that time the United States experienced a comparatively large epidemic of diphtheria and therefore became a leader in the early propaganda for and organization of mass immunization against diphtheria in the postwar period. After Ramon [10] introduced his diphtheria anatoxin, or toxoid, in 1923, the practice of mass immunization received a new impetus not only in the French-speaking countries but in the United States and elsewhere.

In order that the efficiency of these immunizations might be proved, statistical curves were published all over the world which showed a decrease in diphtheria morbidity a few years after the introduction of immunization as compared with a preceding two to five year control period in which there was no immunization. Thus the same mistake was made which had led to hasty conclusions early in the era of antitoxin therapy. Such statistics should be discontinued as unscientific.

The following statement can be made concerning the efficiency of antidiphtheritic immunization on the basis of the secular waves of diphtheria morbidity: According to Schick,[11] in 1931 over 1,000,000 children had been immunized against diphtheria in France, Belgium and Canada. Whatever the number of immunized children might have been at that time in the other European countries, there is no doubt that immunization on the European continent has not been sufficient in scale to prevent or even modify one of the most dreadful waves of diphtheria in recent European history. This does not mean, of course, that the immunization was entirely useless, but it indicates that statistical methods other than that under consideration must be applied to prove the local effectiveness of immunization (see the section on the control series method). The future will show whether large scale immunization performed all over Europe will be able to modify the next wave of diphtheria, due early in the decade 1940 to 1950.

In 1920, during a peak of a wave, immunization against diphtheria was organized for school children in the city of New York and in other places in the United States (Park [12]). Before 1928, 500,000 school children had been immunized in New York. Diphtheria morbidity was low

8. (*a*) Hahn, B.: Verhandl. d. deutsch. Kong. f. inn. Med. **30**:460, 1913. (*b*) Hahn, B., and Sommer, F.: Deutsche med. Wchnschr. **40**:13, 1914.

9. Bieber, W.: Deutsche med. Wchnschr. **46**:1184, 1920.

10. Ramon, G.: Ann. Inst. Pasteur **45**:291, 1930.

11. Schick, B.: Ergebn. d. sozial. Hyg. **1**:146, 1929; Monatschr. f. Kinderh. **51**:454, 1932.

12. Park, W. H.: History of Diphtheria in New York City, Am. J. Dis. Child. **42**:1439 (Dec.) 1931.

from 1923 to 1926, but the next peak of the wave nevertheless occurred in 1927. Therefore, a concerted drive for immunization of preschool children was organized in the city in 1929. Thirty-three per cent of the babies were reached in 1933 and 45 per cent in 1934, and the percentage may now be well over 60. The health officer of New York who prepared and analyzed the secular curve of diphtheria morbidity reproduced in chart 2 made the following critical statement in 1929:[12a] "Apparently we are on the downward slope of a periodic wave which may continue until 1930 or 1931 after which another rise may be expected unless some new factor or factors are introduced." As is seen in the curves both of New York and of the United States, the expected rise in 1931 is hardly noticeable, and the peak of the wave due in 1934 is entirely missing. The new factor introduced in the meantime is probably the large scale immunization of preschool children started in 1929. Therefore, it is certainly fair to admit that the peak of diphtheria morbidity due in 1934 in New York was prevented by the introduction of immunization of preschool children. The same is true of the entire United States. The only objection which might be made against this conclusion lies in the fact that during the period between 1895 and 1935 there was a spontaneous downward trend of diphtheria morbidity in New York. However, the six and one-half year cycle has persisted ever since, except during recent years.

Control Series Method.—The comparatively unimpressive results obtained with the statistical method just discussed do not mean that the efficiency of immunization against diphtheria has not otherwise been sufficiently demonstrated. This has been achieved by the so-called control series method. It consists of comparing, in the same place and at the same time, diphtheria morbidity in a nonimmunized and in an immunized group of children of the same age. This method was used in regard to von Behring's immunization in Magdeburg as reported by Bieber[9] (1920) and in many later statistical reports. Twenty statistical reports of this kind published before 1932, covering about 400,000 immunized children and as many controls, were listed by de Rudder in his remarkable book, "Acute Contagions of Civilization."[13] These statistics, taken by the control series method, prove beyond any doubt that diphtheria morbidity in immunized children is only one third to one eighth, or an even smaller fraction of that of nonimmunized children. This fact has been acknowledged by the most skeptical critics, such as Buergers[14] and Doerr,[15] since it is based on

13. de Rudder, B.: Die akuten Zivilisationsseuchen, Leipzig, Georg Thieme, 1934.

14. Buergers, T. J.: Ergebn. d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap. **17**:231, 1935.

15. Doerr, R.: Klin. Wchnschr. **11**:1409, 1932.

the most reliable statistical method at present available to prove the efficiency of active immunization against diphtheria. Less reliable methods, such as determination of serum antitoxin or application of the Schick test after immunization, though of uncontested value for the purpose of orientation, will not be discussed in this paper.

SEVERITY AND TYPE OF DIPHTHERIA OCCURRING AFTER IMMUNIZATION

A quantitative analysis has been given of the cases of diphtheria occurring in children immunized against diphtheria. Now arises the question of a qualitative analysis of those cases: What is the severity, the clinical typology and the mortality rate of diphtheria in children who were routinely immunized against the disease at least several weeks previously? The general answer to this question is that diphtheria in immunized children is "less severe" than in nonimmunized controls. For many reasons, however, the distinction according to clinical "severity" of mild, medium and severe diphtheria is unsatisfactory. Besides the vagueness of the term "severity," there is, for instance, the disadvantage that under the term of "severe diphtheria" are mixed in one group such different types of the disease as diphtheritic croup and toxic diphtheria. To avoid this confusion I reanalyzed the old clinical typology of Escherich [16] (1895) in my monograph on the typology of diphtheria of the throat.[17] There are three types of the disease: (1) localized diphtheria, which is confined, in the case of pharyngeal localization, to the tonsils or their immediate neighborhood in the throat; (2) progressive diphtheria, usually associated with diphtheritic croup or even with tracheobronchial membranes, with or without involvement of the nose, mouth and pharynx and (3) toxic, or edematous, diphtheria, usually confined to Waldeyer's tonsillar ring and often characterized by a bull-necked appearance.

In the monograph just referred to I attempted to analyze, according to this typology, cases of diphtheria in immunized children as reported in the literature. Unfortunately, in most of the reports either no types of diphtheria are differentiated at all or the classification is made according to "severity." I finally compiled twenty-one articles, representing 897 cases of diphtheria in immunized children, in which the clinical type of diphtheria was expressly stated or could at least be recognized by implication (table 2). Table 3 compares statistics on the clinical typology in these cases with my statistics for 1,191 nonimmunized children in Cologne. The figures show that while toxic diphtheria is about equally frequent in the two groups, localized

16. Escherich, T.: Diphtherie, Croup, Serumtherapie, Vienna, K. Prochaska, 1895; Berl. klin. Wchnschr. **38**:33, 1901.

17. Seckel, H.: Abhandl. a. d. Kinderh., 1937, no. 44.

pharyngeal diphtheria is distinctly more common and diphtheritic croup much rarer in the immunized than in the nonimmunized group. This reduction of dangerous laryngeal diphtheria with an increase of harmless localized pharyngeal diphtheria is the primary factor to make diphtheria in immunized children appear "less severe" than that of the controls. But there is another distinction in favor of the immunized group. The mortality rate in the cases of "severe" involvement, both with diphtheritic croup and with toxic diphtheria, is smaller than for the nonimmunized group. In the literature it is uniformly stressed that laryngeal diphtheria was unusually mild in immunized children and that an operative procedure, such as intubation or tracheotomy, was rarely necessary. In the cases of laryngeal diphtheria listed in table 2, only 2 of 16 patients died, whereas the mortality rate for nonimmunized children is 20 per cent or higher in most of the recent European statistics. On the other hand, among immunized children toxic diphtheria was fatal

TABLE 3.—*Clinical Typology of Diphtheria in Immunized and Nonimmunized Children*

Clinical Types of Diphtheria	897 Immunized Children		1,191 Nonimmunized Children	
	Number of Cases	Percentage	Number of Cases	Percentage
Localized pharyngeal	747	83.1	811*	68.5
Laryngeal	16	1.8	185	15.4
Toxic	134	15.0	195	16.2

* Tonsillar diphtheria plus progressive diphtheria without croup.

in 34 of 134 cases, which corresponds to a mortality rate of 25.4 per cent, as against over 40 per cent in the last European epidemic.

This purely bibliographic study is not free from various sources of error, and it would be of great interest to conduct a large scale investigation on diphtheria in immunized children with this particular typologic problem in mind. Nevertheless, even on the basis of the preliminary material just presented, the pathogenetic problem may be approached: What is the reason for the peculiar shift of diphtheria in immunized children from the laryngeal to the pharyngeal type? In my opinion, this question must be visualized in connection with the problem of the so-called pathomorphosis of diphtheria which occurred in the course of the last forty years. The facts involved are given in chart 3. According to von Bokay's [18] statistics, in 1895 in about 48 per cent of all cases the type of the disease was laryngeal croup and in 52 per cent pharyngeal diphtheria, including an unidentified portion of toxic diphtheria. The corresponding figures of recent years for nonimmunized children are 15.4 per cent diphtheritic croup and 84.7 per cent pharyngeal

18. von Bokay, J.: Ergebn. d. inn. Med. u. Kinderh. **42**:463, 1932; **43**:428, 1932.

diphtheria in Cologne (Seckel;[17] table 3), and 12.3 and 87.7 per cent, respectively, in Budapest (von Bokay[18]). In immunized children, this shift is much more pronounced, as in only 1.8 per cent of the cases is the disease diphtheritic croup and in 98.2 per cent pharyngeal diphtheria. What, again, is the reason for this twofold pathomorphosis?

Since no satisfactory answer to this question has so far been suggested, in my monograph[17] and in a more recent paper[19] I advanced a hypothesis which is summarized in table 4. In this view the often neglected fact is brought into the foreground that the silent contacts with diphtheria bacilli, occurring more and more frequently as childhood advances, not only elicit the production of antitoxin which circulates in the blood but may lead to the accumulation in the tissues of sessile antibodies, which do not overflow into the circulation. The former results in what is commonly referred to as specific immunity, and the latter, in so-called specific sensitization. As long as neither

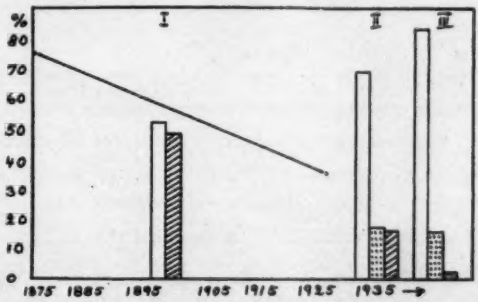

Chart 3.—Pathomorphosis of diphtheria typology; percentage of cases per type from 1895 to 1935. White columns represent localized pharyngeal diphtheria; shaded columns, laryngeal diphtheria, and dotted columns, toxic diphtheria. *I* represents von Bokay's statistics on Budapest, Hungary, from 1895 to 1897 (toxic diphtheria included in white column); *II*, Seckel's statistics on Cologne, Germany, for nonimmunized children from 1932 to 1935; *III*, statistics of immunized children (table 2) from 1929 to 1937. The solid line represents the percentage of Germany's rural population from 1871 to 1925 (Bennholdt-Thomsen, C.: Klin. Wchnschr. **17**:865, 1938; in 1800, 90 per cent; in 1850, 75 per cent).

one develops in early childhood, progressive diphtheria, usually with croup is apt to occur, according to the hypothesis in question. In older children, however, who are either mildly sensitized or hypersensitive to products of diphtheria bacilli and have lost or not yet acquired complete specific immunity, either localized pharyngeal diphtheria or toxic diphtheria with its typical pathologic feature of so-called hypergic inflammation (Roessle[19a]) is to be expected. To explain the spontaneous pathomorphosis of diphtheria on the basis of this theory, I

19. Seckel, H.: Ann. pædiat. **152**:73, 1938.

19a. Roessle, R.: Verhandl. d. deutsch. path. Gesellsch. **17**:281, 1914; **19**:18, 1923; Wien. med. Wchnschr. **82**:215, 1932.

assume that the rapid development of traffic, industrialization and urban growth, as demonstrated by the decrease of rural populations during the last half-century (chart 3), has increased the chances of contacts with diphtheria bacilli in children and therefore of spontaneous sensitization to specific bacterial products. This change in disposition toward diphtheria bacilli from nonsensitivity to mild or severe sensitivity is clinically reflected in a shift from the preschool type of diphtheritic croup to the school types of localized pharyngeal diphtheria and toxic or hypertoxic diphtheria. By the early contacts with diphtheria bacillary products which take place with toxoid immunization in early childhood, an even more general, though milder, sensitization of the body tissues, including the pharynx, is brought about. Consequently, the type of diphtheria in immunized children, by a sort of artificial pathomorphosis, is shifted even more toward the tonsillar and toxic and away from the

TABLE 4.—*Relation of Clinical Type of Diphtheria to Acquired Disposition Toward Diphtheria Bacilli* *

Clinical Type of Diphtheria	Age of Predilection, Years	Frequency of Former Bacillary Contacts	Results of Tests		Type of Inflammation (Roessle)[19a]	Disposition Toward Diphtheria Bacilli
			Schick	Zoeller†		
Progressive	2-7	0 or (+)	++	0	Anergic or hypoergic	Nonsensitivity
Localized	3-10	+	+	+	Normergic	Mild sensitivity
Toxic Hypertoxic	4-13	++	(0)	++	Hyperergic	Hypersensitivity Anaphylaxis

* Seckel, footnotes 17 and 19.
† A test based on specific sensitization to diphtheria bacilli proteins (endotoxins). Results of cutaneous tests refer to the probable reactions before the onset of the disease.

laryngeal variety. In most children, however, particularly in the immunized group, sensitivity is disguised by active immunity, which prevents the disease from becoming manifest. This is shown by the fact that, besides a negative Schick reaction, a more or less strongly positive Zoeller-Moloney reaction (Zoeller,[20] Moloney and Frazer[21]), or pseudo Schick reaction (table 4), with or without exaggerated local or general disturbances, is often found in immunized children (Antonov,[22] Parish,[23] Pohl,[24] Underwood[25]). The same is true of children who have had diphtheria one or two years previously (Baar and Kovacs;[26] for further details see Seckel[27]).

20. Zoeller, C.: Compt. rend. Soc. de biol. **91**:165, 1924; Presse méd. **34**: 659, 1926.
21. Moloney, P. J., and Frazer, C. J.: Am. J. Pub. Health **17**:1027, 1927.
22. Antonov, N. M.: Zentralbl. f. d. ges. Kinderh. **32**:320, 1936.
23. Parish, H. J.: Lancet **2**:310, 1936.
24. Pohl, C.: Ztschr. f. Kinderh. **65**:312, 1936.
25. Underwood, E. A.: J. Hyg. **35**:449, 1935.
26. Baar, H., and Kovacs, N.: Klin. Wchnschr. **16**:1532, 1937.
27. Seckel, footnotes 17 and 19.

NONSPECIFIC PREVENTIVE THERAPY

The recent European wave of diphtheria has presented for treatment an unusually great number of patients with toxic diphtheria. Even in countries with general immunization this type has been not infrequently met with in nonimmunized as well as in immunized children. Under treatment with higher and higher doses of antitoxin, toxic diphtheria, in all European statistics, showed a mortality rate of about 42 per cent, while 80 to 100 per cent died among those with the severest, so-called malignant type. The conclusions drawn from this unsatisfactory experience as to the efficiency of antitoxin treatment of diphtheria were utterly divergent. On the one hand, Hottinger,[28] of Düsseldorf, Germany, in 1932 mentioned "the myth of successful specific treatment," and Zischinsky,[29] of Vienna, Austria, in 1934 came to the conclusion that in practice the so-called specific serum therapy has not withstood the ordeal. On the other hand, clinicians of the pre-Behring era, such as Heubner[30] and von Bokay,[18] and former collaborators of von Behring, such as Kleinschmidt[31] and others, have definitely taken the following stand: Antitoxin therapy most certainly prevents the spread of diphtheria membranes from the nose or pharynx to the larynx and to the deeper air passages[32] and reduces mortality in proportion to earliness of administration. In the treatment of toxic and malignant diphtheria, antitoxin therapy, today as in earlier times, is reaching the natural limits of its preventive powers, since these patients' (hypersensitive) tissue cells already have absorbed the fatal dose of diphtheria toxins before any serum treatment can, as a rule, be expected. In other words, antitoxin therapy is *the* specific prophylactic for progressive diphtheria but is hardly able to prevent or decidedly alter the course of toxic diphtheria.

Under these circumstances, the radical as well as the conservative experts have tried to overcome the natural limits of antitoxin treatment of toxic diphtheria by devising new methods of nonspecific preventive therapy. Two examples of such treatment will be discussed: (1) parenteral protein therapy and (2) intravenous injections of dextrose.

Parenteral Protein Therapy.—In a clinical review on this subject Kleinschmidt[33] wrote in 1937:

> The problem of so-called toxic diphtheria changes face completely if it is considered that . . . (according to Seckel's hypothesis) toxic diphtheria is caused

28. Hottinger, A.: Abhandl. a. d. Kinderh., 1932, no. 31.
29. Zischinsky, H.: Abhandl. a. d. Kinderh., 1934, no. 36.
30. Heubner, O.: Klinische Studien über die Behandlung der Diphtherie, Leipzig, J. A. Barth (A. Meiner), 1895.
31. Kleinschmidt, H.: München. med. Wchnschr. **82**:1143, 1935.
32. This causes only a certain part of diphtheritic pathomorphosis.
33. Kleinschmidt, H.: Monatschr. f. Kinderh. **68**:24, 1937.

by an increased affinity to diphtheria toxin of sensitized tissues, i. e. by a state of hyperergic reactivity of the organism. Following this assumption it is easily understood why certain efforts to improve the efficiency of the serum (by using "humanized" antitoxin) have failed. . . . If the view is taken that in toxic diphtheria one is dealing with a hypersensitivity reaction it is inevitable to draw the corresponding therapeutic conclusions. It is remarkable that, although unconsciously, a treatment analogous to that of allergic diseases, namely, parenteral nonspecific protein therapy using proteins foreign as to species or individuals, has increasingly been applied in various forms as an additional procedure.

First of all, the successful infusion of ever higher doses of diphtheria antitoxin up to 1,000,000 units per patient has been considered not so much a superior specific treatment with antitoxin but an additional nonspecific treatment with foreign proteins. The same holds true of additional injections of antistreptococcus serum or of other serums used in the treatment of toxic diphtheria. On the basis of this interpretation, Hottinger and Toepfer [34] proposed the "nonspecific potentiation of specific serum treatment," consisting of repeated daily injections, besides the initial injection of antitoxin, of small doses of plain horse serum for four to six days. Furthermore, Schultz [35] observed beneficial effects of severe serum disease in cases of toxic diphtheria treated with antitoxin. From this experience, he proceeded to a new fever treatment of toxic diphtheria consisting of parenteral injections of plant proteins ("pyrifer"). Finally, Baar and Benedict [36] introduced into the treatment of toxic diphtheria a single transfusion of 250 to 450 cc. of human blood along with the initial injection of a medium-sized dose of specific antitoxin. With this method I have treated 34 patients with severely toxic, "malignant" diphtheria; [37] in all, some 150 cases are on record in the literature.

All investigators using the various methods of nonspecific parenteral protein therapy have claimed to have reduced the mortality rate of toxic diphtheria from about 42 per cent to between 25 and 35 per cent and that of severely toxic, "malignant" diphtheria from at least 80 to about 40 per cent. Besides, the course of the disease has been favorably influenced by the new procedures, which have insured better general conditions, alleviation of myocarditis and prevention of fatal respiratory palsies. In Kleinschmidt's [33] experience, blood transfusion and "nonspecific potentiation" are of the same value.

Intravenous Injections of Dextrose.—The purpose of this therapy is to reduce the mortality rate of toxic diphtheria by preventing or mitigat-

34. Hottinger, A., and Toepfer, D.: Ztschr. f. Kinderh. **54**:505, 1933.
35. Schultz, W.: München. med. Wchnschr. **81**:567, 1934.
36. Baar, H., and Benedict, H.: Klin. Wchnschr. **11**:1549, 1932.
37. Seckel, H.: Med. Klin. **31**:1603, 1935.

ing myocarditis and hepatic damage. In 1925 Edmunds and co-workers [38] showed that in dogs almost dying of diphtheritic intoxication, intravenous injections of a 10 per cent solution of dextrose immediately raised the blood pressure and improved the action of the heart: "The effect of the dextrose was truly life saving." This procedure, besides injections of antitoxin (up to 50,000 units) was introduced into the treatment of toxic diphtheria by various clinicians. Outstanding among them was Hoyne.[39] In a first series of cases (1934) Hoyne,[39a] as did others before him, started the dextrose treatment after the clinical picture of myocarditis had already developed, that is, in the second week of the disease. Of 112 patients with severe myocarditis, 10 recovered and 102 died, a proportion of recovery which is, of course, no unusual achievement. However, in a second series of cases [39b] the dextrose therapy was transformed by Hoyne into a truly preventive measure by being started immediately after admission to the hospital for the following four groups of patients: (1) those ill more than three days prior to receiving antitoxin; (2) those with "bull neck" types, irrespective of the day in the course of the disease that antitoxin was injected; (3) patients with marked albuminuria; (4) all patients with the postnasal type or with a malignant type of any character. Five hundred cubic centimeters of a 10 per cent solution of dextrose was given daily to children and 1,000 cc. to adults for about nine days. Of a series of 81 "critical diphtheria patients" admitted to the hospital as late as the end of the fifth day of illness, only 8 patients died. This corresponds to a mortality rate of 10 per cent, as against an expected fatality of 30 to 60 per cent with no dextrose treatment. Myocarditis, it is believed, has often been prevented by this type of treatment. Even if it is admitted that not all of these patients with "critical" illness had toxic or malignant diphtheria in the proper sense, this result is nevertheless imposing. In my opinion, injections of dextrose should be used in combination with one of the methods of parenteral protein therapy in all cases of severely toxic diphtheria.

The value of injections of ascorbic acid and extract of adrenal cortex in cases of toxic diphtheria is obviously not yet proved. Besides a reduction of hemorrhagic manifestations, there seems to be no influence on either mortality or severeness of complications (Dieckhoff and Schüler,[40] 1938).

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38. Edmunds, C. W., and Cooper, R. G.: Action of Cardiac Stimulants in Circulatory Failure Due to Diphtheria, J. A. M. A. **85**:1798 (Dec. 5) 1925. Edmunds, C. W., and Johnston, F. D.: Circulatory Collapse in Diphtheria, J. A. M. A. **90**:441 (Feb. 11) 1928. Edmunds, C. W.; Cooper, R. G., and Johnston, F. D.: Am. Heart J. **4**:16, 1928. Edmunds, C. W.: Circulatory Collapse in Diphtheria (Henry Russell Lecture), Am. J. Dis. Child. **54**:1066 (Nov.) 1937.

39. Hoyne, A. L.: (*a*) J. Pediat. **5**:642, 1934; (*b*) Am. J. M. Sc. **191**:271, 1936.

40. Dieckhoff, J., and Schüler, K.: Klin. Wchnschr. **17**:936, 1938.

SUMMARY

In conclusion, the questions brought up at the beginning of this review may be answered as follows:

1. The best statistical method of checking the efficiency of active immunization against diphtheria is the so-called control series method. It has been proved by this method that diphtheria morbidity in immunized children is only one third to one eighth or an even smaller fraction of that of nonimmunized children. Another statistical method is discussed which compares diphtheria morbidity in a given area before and after the introduction of immunization. This method should not be used for scientific purposes except against the background of the secular waves of diphtheria morbidity, which are given for several European cities and for New York from the end of the last century. The only fact to be demonstrated by this method is the lack, in New York and in the United States, of the peak of a diphtheria wave, which was due in 1934, after large scale immunizations of preschool children had been introduced in 1929.

2. In general, the "severity" of diphtheria in immunized children is less than in the nonimmunized controls. If the clinical typology of diphtheria in immunized children is analyzed statistically (according to Escherich's types), there is found an overwhelming majority of cases of localized pharyngeal diphtheria, an almost complete disappearance of diphtheritic croup and about the same percentage of cases of toxic diphtheria as for nonimmunized children. The last two types of severe diphtheria are clinically less alarming in immunized children than they are in the control groups. This artificial pathomorphosis of types of diphtheria following active immunization exaggerates even further spontaneous pathomorphosis, which has reduced diphtheritic croup in favor of pharyngeal diphtheria during the last decades. Both phenomena are explained on the basis of my allergy hypothesis of the clinical typology of diphtheria.

3. Antitoxin therapy is the classic preventive for progressive diphtheria, while it reaches the natural limits of its preventive efficiency in cases of toxic and malignant diphtheria. These limits may be in part overcome by two groups of nonspecific preventive treatment: (1) parenteral protein therapy, consisting of injections of huge doses of foreign serum, irrespective of its specific antibody content, repeated small doses of plain foreign serum or plant proteins or large amounts of human blood, transfused simultaneously with the initial injection of diphtheria antitoxin, and (2) intravenous dextrose therapy, consisting of large infusions of a 10 per cent solution of dextrose for several days, starting immediately after the patient's admission. Both types of nonspecific treatment are routinely combined with the injection of medium-sized doses of diphtheria antitoxin and may, in cases of malignant diphtheria, be combined with each other.

OLD TUBERCULIN AND PURIFIED PROTEIN DERIVATIVE IN THE TUBERCULIN PATCH TEST

A COMPARATIVE STUDY

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With a view to further improving the tuberculin patch test, purified protein derivative was substituted for old tuberculin. Purified protein derivative was supplied in a 1 per cent solution by the Henry Phipps Institute, Philadelphia, with the information that this solution has the same strength as a standard preparation of old tuberculin. According to several authors, this product is superior to old tuberculin.

METHOD

Filter papers were saturated with old tuberculin from the New York State Department of Health and with purified protein derivative, respectively; they were then dried and cut into squares measuring 1 by 1 cm. One of each kind of these squares was pasted on every adhesive strip. In this way ideal conditions for a comparative study were obtained, since the two products were applied in the same concentration, at the same time, on the same area of skin of the same subject. These combined patch tests were applied for only twenty-four hours.

RESULTS

Comparative studies made on 130 children of the Sea View Hospital yielded the following results:

Number of Children	Percentage of Children	Old Tuberculin	Purified Protein Derivative
69	53.1	Positive	Positive
31	23.8 [1]	Negative	Negative
27	20.8	Positive	Negative
3	2.3	Negative	Positive

Of 130 children, 100, or 76.9 per cent, showed conformity in their reactions to old tuberculin and to purified protein derivative. Of the 30

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1. This high incidence of negative reactions is due to the short application time of the patch tests and to the use of regular old tuberculin instead of the synthetic old tuberculin which is used in the Lederle tuberculin patch test.

children, or 23.1 per cent, whose reactions did not correspond, 27, or 20.8 per cent, reacted positively to old tuberculin and negatively to purified protein derivative and only 3, or 2.3 per cent, showed a positive reaction to purified protein derivative and a negative reaction to old tuberculin.

COMMENT

These figures indicate that in the tuberculin patch test old tuberculin is decidedly superior to purified protein derivative, a fact which we cannot satisfactorily explain. A possible explanation may lie in the solubility of both types of tuberculin. The skin obviously reacts only to tuberculin in solution, not to the dry substance. Old tuberculin always contains water, owing to its high content of hydrophile glycerin, particularly when it is exposed to the air. This water content insures an immediate reaction from the moment of contact, a reaction which is enhanced by further dilution of the old tuberculin through the insensible perspiration. This is not the case, however, with purified protein derivative. The 1 per cent solution, once dried in the filter paper, is and remains practically free of water until the moment of its application. It therefore takes a relatively longer time for the insensible perspiration to dilute the purified protein derivative and thus make a cutaneous reaction possible. In addition to this factor, a difference in absorption of the two products through the skin may also play a role.

We do not mean to suggest that these results concern the effectiveness of purified protein derivative as applied in the Mantoux intracutaneous test. However, they induced us to use old tuberculin exclusively for the tuberculin patch test.

NOTE.—This study was completed in 1937, but its publication has been delayed.

25 Central Park West, New York.

Sea View Hospital, Staten Island, N. Y.

INFLUENCE OF FLUID AND OF EVAPORATED MILK ON MINERAL AND NITROGEN METABOLISM OF GROWING CHILDREN

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DETROIT

The newer knowledge of nutrition and modern methods of manufacture are gradually dispelling prejudices against canned foods. The widespread use of evaporated milk for infants attests its ability to nourish them well. The fact that infants are unable to digest raw cow's milk properly is largely overcome by boiling or by the processes used in the production of evaporated milk.[1] Moreover, this modified cow's milk lends itself to a degree of standardization and control unapproachable with the mammary gland. The main objection to this milk product, unpalatability, appears more psychologic than real when tested in the light of unprejudiced experience.[2] Evaporated milk is recommended by the fact that it is uniform in composition, is sterile and requires no refrigeration. From the economic standpoint, its cost is comparatively low and the supply readily available. As this milk product is generally accepted as the basis of the artificial feeding formulas of infants, the question of whether its efficiency in promoting the growth and mineral

From the Research Laboratory, Children's Fund of Michigan, in cooperation with the Methodist Children's Village.

This study was aided by grants from the Wisconsin Alumni Research Foundation, Madison, Wis., and the United Fruit Company, Boston.

1. (*a*) Marriott, M., and Schoenthal, L.: An Experimental Study of the Use of Unsweetened Evaporated Milk for the Preparation of Infant Feeding Formulas, Arch. Pediat. **46**:135, 1929. (*b*) Jeans, P. C., and Stearns, G.: Growth and Retentions of Calcium, Phosphorus and Nitrogen of Infants Fed Evaporated Milk, Am. J. Dis. Child. **46**:69 (July) 1933.

2. Hollinger, M., and Roberts, L. J.: Overcoming Food Dislikes: A Study with Evaporated Milk, J. Home Econ. **21**:923, 1929.

retention of developing children is equal to that of fresh whole milk is a problem worthy of further scientific investigation.[3] The present study is concerned with the relative efficiency of plain fluid and of evaporated milk in meeting the mineral and nitrogen demands of the growing child.

MATERIAL AND METHODS

The nitrogen and acid-base mineral balance study was conducted on 3 healthy growing children who received a basal diet which conformed with accepted nutritive standards and was fed in quantities sufficient to meet the caloric and protein needs of each child. The diet was composed of inexpensive foods readily available throughout the year.[4] Each child's daily ration was weighed out in the morning, and the day's meals were ingeniously prepared from various combinations of these portions by three trained workers. These workers, who lived in the home with the children and their house mother, supervised the intake of food, made the metabolic collections and recorded measurements of growth, activity and emotional reaction. The diet was prepared in identical manner for the laboratory analyses, which were made at frequent intervals.[5]

All milk used during the study was obtained from the same herd of cows, and each type of milk was subjected to uniform methods of collection, handling and processing, rigidly controlled [6] to assure a supply of unvarying quality throughout each diet period.[7] Each child received 400 Gm. of plain fluid milk daily for twenty-five to forty days (one hundred experimental days). During the following twenty to twenty-five days (seventy experimental days) the same quantity of plain evaporated milk (diluted 1:1) was included in the diet. Finally, for the twenty-five days immediately following (seventy-five experimental days) each child

3. Daniels, A. L., and Stearns, G.: The Effect of Heat Treatment of Milk Feedings on the Mineral Metabolism of Infants, J. Biol. Chem. **61**:225, 1924. Willard, A. C., and Blunt, K.: A Comparison of Evaporated with Pasteurized Milk as a Source of Calcium, Phosphorus and Nitrogen, ibid. **75**:251, 1927. Kramer, M. M.; Latzke, E., and Shaw, M. M.: A Comparison of Raw, Pasteurized, Evaporated, and Dried Milks as Sources of Calcium and Phosphorus for the Human Subject, ibid. **79**:283, 1928.

4. The basal diet was composed of apple, banana, beef, white and whole wheat bread, butter, cabbage, carrots, cheese, eggs, graham crackers, lettuce, milk, peanut butter, potato, shredded wheat or corn flakes, tomato and orange juice, sugar and salt.

5. Complete, detailed descriptions of the chemical methods will be published in a monograph on the chemical growth of children (in preparation).

6. Mr. C. G. Reichle, plant manager of the Detroit Branch of Borden Farm Products Company of Michigan, controlled the handling of all the milk used in this study.

7. The average composition of milk in grams per hundred grams (irradiated and nonirradiated milk had the same average chemical composition) was as follows:

Milk	Nitrogen	Calcium	Magnesium	Sodium	Potassium	Phosphorus	Chlorine	Sulfur	Iron	Fat
Fluid.....	0.492	0.118	0.012	0.048	0.148	0.089	0.108	0.027	0.00004	3.10
Evaporated (diluted 1:1)..	0.508	0.130	0.013	0.071	0.151	0.108	0.106	0.035	0.00006	3.92

received an identical quantity of irradiated evaporated milk (diluted 1:1). Thus, the only changes in the dietary of the children during consecutive balance periods totaling seventy-five to eighty-five days for each child (two hundred and forty-five experimental days) were the substitution of plain evaporated for plain fluid milk and the replacement of plain evaporated by irradiated evaporated milk.

Frequent periodic assays were made of the vitamin D content of the three types of milk.[8] Both the fluid and the evaporated milk were assayed for their vitamin D content. The irradiated evaporated milk (prepared from one batch of raw milk) contained 203 U. S. P. units (approximately) per 14½ ounce can. The vitamin D supplement obtained by the change from nonirradiated to irradiated evaporated milk was 90 U. S. P. units.

The subjects of this study had been living under the same metabolic regime and had been ingesting a similar diet for sixty-five days before they took the plain fluid milk. Each child received a quart of milk daily for three months before the experimental period, in order to insure well filled mineral stores; it has been amply demonstrated[9] that the nutritive background of a person influences subsequent utilization of minerals, particularly of calcium. The selection of the children by medical history, physical examination[10] and evaluation of skeletal development,[11] the determination of their physical status and well-being, the general care and handling of subjects during the experiment and the methods used in sampling have been described elsewhere.[12] The facilities made available at the Methodist Children's Village made it possible to maintain accurate control in a physical and a mental environment which compared favorably with those of an adequate home; the children slept, studied and played in light, cheery quarters or in the spacious grounds; they were content with their meals and were attached to their supervisors.

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8. The vitamin D tests were made at periodic intervals by the Wisconsin Alumni Research Foundation under the supervision of Henry T. Scott, Ph.D., and independently by C. A. Hoppert, Ph.D., Michigan State College, East Lansing, Mich.

9. Fairbanks, B. W., and Mitchell, H. H.: The Relation Between Calcium Retention and the Store of Calcium in the Body, with Particular Reference to the Determination of Calcium Requirements, J. Nutrition **11**:551, 1936. Rottensten, K. V.: The Effect of Body Stores on the Efficiency of Calcium Utilization, Biochem. J. **32**:1285, 1938. Outhouse, J.; Kinsman, G.; Sheldon, D.; Twomey, I.; Smith, J., and Mitchell, H. H.: The Calcium Requirements of Five Pre-School Girls, J. Nutrition **17**:199, 1939.

10. Marsh W. Poole, M.D., attending physician at the Methodist Children's Village, made the medical examinations and the physical measurements and was responsible for the care of the children's health.

11. The late T. Wingate Todd, M.D., and C. C. Francis, M.D., Western Reserve University, evaluated and studied the skeletal maturity of all the children considered, particularly those finally chosen for the metabolic study.

12. Hummel, F. C.; Hunscher, H. A., and Macy, I. G.: The Influence of Fluid Irradiated and Evaporated Irradiated Milks on the Storage of Nitrogen and Acid-Base Minerals in Children, Am. J. Dis. Child., to be published.

TABLE 1.—*Average Daily Intake and Retention of Children Given 400 Grams Daily of Fluid or Evaporated Milk* *

Child	Type of Milk	Length of Study,† Days	Initial Age, Mo./Days	Caloric Intake per Kg.	Nitrogen, Mg./Kg.		Calcium, Mg./Kg.		Magnesium, Mg./Kg.		Sodium, Mg./Kg.		Potassium, Mg./Kg.		Phosphorus,‡ Mg./Kg.		Sulfur, Mg./Kg.		Chlorine, Mg./Kg.		Fat, Gm./Kg.	
					Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention	Intake	Retention
R. S.	Fluid	40	67/21	101.3	537.9	18.0	40.5	4.2	15.5	1.6	110.3	5.9	147.7	11.1	56.1	6.8	35.7	2.0	182.7	17.0	3.92	3.80
	Evaporated	20	69/ 0	98.6	520.4	29.8	41.4	5.3	15.1	1.2	110.8	4.2	142.7	11.8	57.7	5.6	36.0	2.7	175.3	10.4	3.94	3.82
	Irradiated evaporated	25	69/24	97.7	515.9	34.9	41.0	5.1	15.0	1.5	109.8	7.0	141.4	18.9	57.2	4.1	35.7	2.9	173.8	18.2	3.90	3.76
B. M.	Fluid	25	65/ 6	93.8	533.1	21.1	41.7	7.8	15.1	1.5	101.8	5.6	151.3	12.8	54.7	5.6	34.3	1.8	168.3	16.0	3.50	3.42
	Evaporated	25	66/15	94.7	532.4	51.6	44.0	10.3	15.3	1.4	106.3	3.6	150.8	11.3	58.5	9.7	35.9	3.1	166.6	8.2	3 66	3.57
	Irradiated evaporated	25	67/ 9	91.8	513.4	33.4	42.5	9.6	14.7	1.4	102.5	4.2	145.4	15.2	56.4	3.9	34.7	1.4	160.6	14.2	3.53	3.42
J. H.	Fluid	35	57/21	109.1	580.2	20.4	43.6	6.3	16.6	2.4	119.0	7.3	159.3	9.0	60.5	7.2	38.5	2.3	197.0	23.5	4.23	4.14
	Evaporated	25	59/ 0	105.7	556.2	47.3	44.2	5.6	16.1	1.6	118.4	7.6	152.5	11.0	61.7	7.3	38.5	3.4	187.4	17.0	4.21	4.12
	Irradiated evaporated	25	59/24	102.8	543.9	45.1	43.2	9.5	15.8	1.9	115.8	8.9	149.2	16.3	61.3	5.7	37.7	2.4	183.2	21.0	4.12	4.02
M ± SEM§	Fluid	100	....	.....	551.5± 5.0	19.6± 3.3	41.9± 0.2	5.8± 0.6	15.8± 0.2	1.8± 0.3	111.2± 1.6	6.3± 0.7	152.7± 1.2	10.8± 1.2	57.3± 0.5	6.0± 0.7	36.3± 0.5	2.0± 0.3	184.1± 2.6	19.0± 1.6		
	Evaporated	70	....	.....	537.5± 4.2	43.8± 6.0	43.3± 0.6	7.2± 0.9	15.5± 0.3	1.4± 0.2	111.9± 1.6	5.2± 1.1	149.1± 1.2	11.3± 1.4	59.4± 0.3	7.7± 0.9	36.9± 0.2	3.1± 0.3	176.5± 2.5	12.0± 2.0		
	Irradiated evaporated	75	....	.....	524.4± 3.9	37.8± 4.4	42.2± 0.3	8.1± 0.6	15.2± 0.1	1.6± 0.1	109.4± 1.5	6.7± 0 8	145.4± 0.8	16.8± 1.4	58.0± 0.5	4.6± 1.0	36.0± 0.4	2.2± 0.3	172.6± 2.5	17.8± 1.1		

* 200 Gm. of evaporated milk diluted 1:1 with water.

† Five day balance periods.

‡ The valence of 1.8 is used in the calculation of phosphorus. (Shohl, A. T.; Mineral Metabolism in Relation to Acid-Base Equilibrium, Physiol. Rev. **3**: 509, 1923.)

§ Mean plus or minus standard error of mean.

RESULTS

Table 1 presents the values for the caloric intake and for the average daily intakes and retentions of fat, nitrogen and the acid-base minerals per kilogram of body weight.[5] The intake and retention of fat, while significant in other phases of the chemical growth of these children, apparently were not affected by the type of milk ingested.[13] Ninety-six per cent (or more) of the fat intakes were retained by the children during this study. As for the basic elements (calcium, magnesium, sodium and potassium), when an equal quantity of evaporated milk (diluted 1:1) was substituted for fluid milk, 2 children (R. S. and B. M.) increased their daily retention of calcium per kilogram of body weight from 4.2 to 5.3 mg. and from 7.8 to 10.3 mg. respectively; 1 child (J. H.) showed a decrease from 6.3 to 5.6 mg. When the vitamin D value of the evaporated milk was enhanced by irradiation, all the children retained more calcium than with the plain fluid milk. Two of the children (R. S. and B. M.), however, retained less calcium with the irradiated than with the nonirradiated evaporated milk. As a group, the children retained daily a mean[14] of 5.8 mg. of calcium per kilogram of body weight during the hundred days of ingesting plain fluid milk, 7.2 mg. during the seventy days of ingestion of plain evaporated milk and 8.1 mg. during the seventy-five days of ingestion of irradiated evaporated milk. The 3 children stored slightly more magnesium daily (mean, 1.8 mg. per kilogram) with plain fluid than with evaporated milk (mean, 1.4 mg. per kilogram). When irradiated evaporated milk was given, the mean retention was intermediate, being 1.6 mg. per kilogram. The children showed no consistent differences in retention of sodium with the various types of milk. However, the retention of potassium was considerably higher with irradiated evaporated milk (mean, 16.8 mg. per kilogram) than with fluid milk (mean, 10.8 mg. per kilogram) or with nonirradiated evaporated milk (mean, 11.3 mg. per kilogram). The increased retentions of potassium during ingestion of both types of evaporated milk (nonirradiated and irradiated) indicates a more rapid rate of tissue synthesis with evaporated milk.

A consideration of the acidic elements (phosphorus, sulfur and chlorine) reveals that while there was no consistent trend of phosphorus retentions during the ingestion of plain fluid and plain evaporated milk, all the children retained less phosphorus when taking irradiated evaporated milk. The mean daily phosphorus retentions per kilogram of body weight were 6.6 mg. for the plain fluid milk, 7.7 mg. for the plain evaporated milk and 4.6 mg. for the irradiated evaporated milk.

13. Fat Excretion of Children (in preparation).

14. Means and standard deviations were derived from the total number of average daily figures for the total experimental days of all 3 children.

A higher retention of chlorine (mean, 19 mg. per kilogram) was shown by each of the 3 children during ingestion of plain fluid milk than with evaporated milk (mean, 12 mg. per kilogram). When irradiated evaporated milk was given, 1 child's retention increased above the level of the two previous experimental periods, but the mean of the daily chlorine retentions per kilogram was intermediate (17.8 mg.). All the children retained more sulfur per kilogram daily (mean, 3.1 mg.) while taking plain evaporated milk than while taking plain fluid milk (mean, 2 mg.). When irradiated evaporated milk was given, the mean retention of sulfur (2.2 mg.) was intermediate, although 1 child (B. M.) retained least during this period.

The parallel changes in sulfur and nitrogen retention which occurred with the different types of milk were striking when the evaporated milk replaced plain fluid milk. The mean daily storage of nitrogen per kilogram was 19.6 mg. with plain fluid milk and 43.8 mg. with plain evaporated milk. While the mean nitrogen retention per kilogram for the group was less with irradiated (37.8 mg.) than with the nonirradiated evaporated milk, still a greatly enhanced nitrogen deposit was maintained during intake of both types of evaporated milk.

The data on the calcium, phosphorus, nitrogen and sulfur retentions are shown graphically in the chart. The dotted line, representing the daily retentions per kilogram as obtained from the average for each five day balance period, is superimposed on the mean daily retentions for the total experimental period with each type of milk (shown as a solid line). The wide fluctuations during consecutive balance periods illustrate the physiologic inconstancy of children, which is occasioned by change in the growth impulse, and substantiate the view [15] that continuous long time observations are necessary for proper interpretations of the effect of dietary factors on growth and metabolism. The parallelism between the nitrogen and the sulfur retentions, as well as the greater utilization of nitrogen from evaporated milk, are clearly revealed in the chart.

It is apparent that the increased nitrogen, sulfur and potassium retentions (table 1) which occurred during ingestion of evaporated milk are contingent on the percentage of nitrogen intake utilized (table 2) and that they indicate an increase in the synthesis of soft tissue. When ingesting plain fluid milk the children utilized approximately 4 per cent of their nitrogen intake, whereas with the evaporated milks the percentage was more than doubled in some cases, being 6.5 to 10.68 with the nonirradiated and 7.25 to 9.36 with the irradiated type. While it is

15. Hunscher, H. A.; Hummel, F. C., and Macy, I. G.: Variability of Metabolic Response of Different Children to a Given Intake of Calcium, Proc. Soc. Exper. Biol. & Med. **35**:189, 1936.

definitely shown in table 1 and in the chart that the children were able to deposit more nitrogen when ingesting evaporated milk, certain other

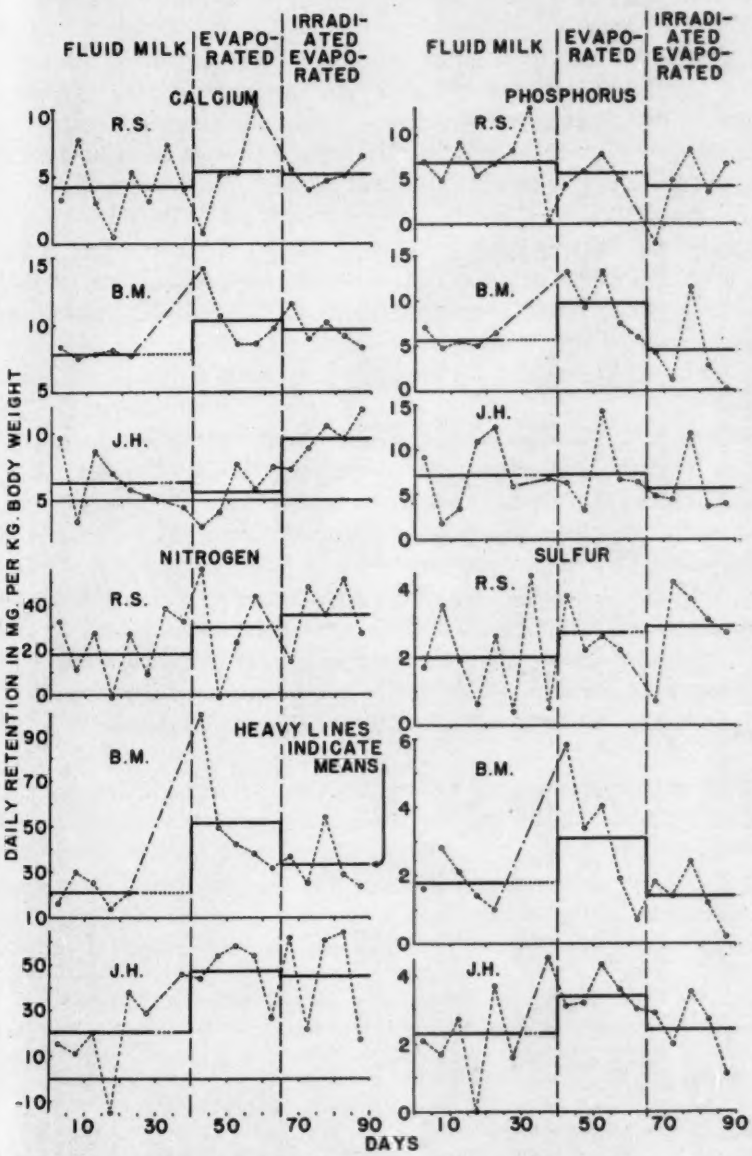

Chart illustrating differences in retention of calcium, phosphorus, nitrogen and sulfur during ingestion of different types of milk.

subtle differences not made obvious by figures for retention are brought out by the data in table 2, as well as by coordinated studies of the gastro-intestinal motility of these subjects and by serial roentgenograms of

TABLE 2.—*Range and Percentage of Retention of Nitrogen, Calcium and Phosphorus During the Consumption of Four Hundred Grams Daily of Fluid or Evaporated * Milk*

Child	Type of Milk	Length of Study,† Days	Initial Date of Study	Recumbent Length: Initial, Cm.	Recumbent Length: Daily Gain, Cm.	Weight: Initial, Kg.	Weight: Daily Gain, Kg.	Nitrogen: Retention, Mg./Kg./24 Hr.: Minimum	Nitrogen: Retention, Mg./Kg./24 Hr.: Maximum	Nitrogen: R/I,§ Percentage	Nitrogen: R/A.,‡§ Percentage	Calcium: Retention, Mg./Kg./24 Hr.: Minimum	Calcium: Retention, Mg./Kg./24 Hr.: Maximum	Calcium: R/I, Percentage	Phosphorus: Retention, Mg./Kg./24 Hr.: Minimum	Phosphorus: Retention, Mg./Kg./24 Hr.: Maximum	Phosphorus: R/I, Percentage	Calcium-Phosphorus Ratio: Intake	Calcium-Phosphorus Ratio: Retention	Potassium-Sodium Ratio: Intake	Potassium-Sodium Ratio: Retention	Minerals, Base Minus Acid: Intake, mEq./Kg./24 Hr.	Minerals, Base Minus Acid: Retention, mEq./Kg./24 Hr.
R. S.	Fluid	40	12/ 4/35	115.0	0.022	18.32	0.0245	—1.6	37.6	3.38	3.82	0.5	7.6	10.48	0.3	12.9	12.05	0.72	0.62	1.34	1.88	1.23	—0.11
	Evaporated	20	1/13/36	115.9	0.015	19.30	0.0090	—1.5	55.4	5.73	6.50	0.7	10.2	12.81	4.3	7.7	9.78	0.72	0.95	1.29	2.81	1.23	0.06
	Irradiated evaporated	25	2/ 7/36	116.3	0.028	19.50	0.0088	14.4	50.7	6.72	7.73	4.0	6.4	12.46	—2.2	8.1	7.20	0.72	1.24	1.29	2.70	1.22	0.24
B. M.	Fluid	25	12/ 4/35	105.9	0.024	17.21	0.0116	13.8	29.5	4.00	4.39	7.4	8.3	18.78	4.6	7.0	10.28	0.76	1.39	1.48	2.28	1.55	0.20
	Evaporated	25	1/13/36	106.7	0.012	17.27	0.0240	31.6	99.0	9.66	10.68	8.5	14.1	23.37	5.9	13.1	16.62	0.75	1.06	1.42	3.14	1.60	0.09
	Irradiated evaporated	25	2/ 7/36	107.0	0.032	17.87	0.0208	23.4	53.9	6.54	7.25	8.2	11.5	22.46	0.1	11.4	6.87	0.75	2.46	1.42	3.62	1.54	0.44
J. H.	Fluid	35	12/ 4/35	107.5	0.018	16.96	0.0240	—15.5	45.7	3.58	3.97	3.4	9.6	14.36	1.8	12.5	11.82	0.72	0.88	1.34	1.23	1.33	—0.16
	Evaporated	25	1/13/36	108.2	0.016	17.92	0.0232	26.5	58.2	8.50	9.54	3.0	7.6	12.61	3.2	14.2	11.85	0.72	0.77	1.29	1.45	1.32	—0.10
	Irradiated evaporated	25	2/ 7/36	108.6	0.024	18.50	0.0088	17.1	64.2	8.30	9.36	7.3	11.6	22.09	3.6	11.7	9.45	0.72	1.67	1.29	1.83	1.29	0.35

SD ± SE of SD #	Intake	Nitrogen	Calcium	Phosphorus
	Fluid (100)	22.4 ± 3.5	0.7 ± 0.1	2.2 ± 0.3
	Evaporated (70)	15.9 ± 3.0	2.3 ± 0.4	1.3 ± 0.2
	Irradiated evaporated (75)	15.1 ± 2.8	1.1 ± 0.2	1.8 ± 0.3
	Retention			
	Fluid (100)	14.6 ± 2.3	2.5 ± 0.4	3.2 ± 0.5
	Evaporated (70)	22.6 ± 4.3	3.4 ± 0.6	3.4 ± 0.6
	Irradiated evaporated (75)	17.2 ± 3.1	2.5 ± 0.4	3.8 ± 0.7

* 200 Gm. of evaporated milk diluted 1:1 with water.

† Five day balance periods.

‡ Coefficient of utilization (Gordon, H. H.; Levine, S. Z.; Wheatley, M. A., and Marples, E.: Respiratory Metabolism in Infancy and in Childhood: XX. The Nitrogen Metabolism in Premature Infants—Comparative Studies of Human Milk and Cow's Milk, Am. J. Dis. Child. **54**: 1030 [Nov.] 1937).

§ R/I signifies proportion of retention to intake; R/A. proportion of retention to absorption.

Standard deviation plus or minus standard error of standard deviation.

the progress of barium sulfate in various mediums through the gastrointestinal tract.[16]

Two factors are involved in this study, namely, a change from plain fluid to evaporated milk and enhanced intake of vitamin D. While it is evident from the data on nitrogen metabolism that evaporated milk produced greater synthesis of soft tissue (muscular, neural and glandular), the effect of increased vitamin D intake is less conspicuous.[17] All the children showed a greater utilization of calcium with the irradiated evaporated milk (12.46 to 22.46 per cent) than with the plain fluid milk (10.48 to 18.78 per cent); however, 2 of the children (B. M. and R. S.) retained a slightly larger percentage of their calcium intake with the plain evaporated than with the irradiated evaporated milk. All the children retained less of their phosphorus intake (6.87 to 9.45 per cent) with the irradiated evaporated milk than with the nonirradiated evaporated milk (9.78 to 16.62 per cent) or the plain fluid milk (10.28 to 12.05 per cent).

The calcium-phosphorus ratios of the retentions indicate stimulation of the rate of bone development in comparison with the rate of soft tissue formation as the result of additional vitamin D. During ingestion of plain fluid milk the children had retention ratios (calcium: phosphorus) ranging from 0.62 to 1.39; with evaporated milk ratios ranged from 0.77 to 1.06, whereas with irradiated evaporated milk they were 1.24 to 2.46. A retention ratio of 1.5 is considered to indicate equal rates of formation of skeletal and of soft tissue; if the ratio is less than 1, the soft tissues are growing more rapidly, whereas a ratio greater than 2 is indicative of rapid skeletal growth as compared with soft tissue synthesis.[18]

Although the children showed continuous gains in weight throughout the experiment (table 2), there was no evident relation between these gains and the more rapid rate of soft tissue or of bone development at different periods. All the children, however, showed a more rapid gain in recumbent length coincident with the supplementary vitamin D intake,[19] which supports the conclusion that the increased

16. Macy, Icie G.; Reynolds, L., and Souders, H. J.: The Effect of Carmine Upon the Gastrointestinal Motility of Children, Am. J. Physiol. **126**:75, 1939. Reyenolds, L.; Macy, I. G., and Souders, H. J.: A Comparison of Pasteurized, Evaporated and Base-Exchanged Milks on the Rate of Gastrointestinal Motility of Children, J. Pediat., to be published.

17. Drake, T. G. H.; Tisdall, F. F., and Brown, A.: Irradiated Evaporated Milk in the Prevention of Rickets, J. Pediat. **8**:161, 1936.

18. Stearns, G.: The Significance of the Retention Ratio of Calcium: Phosphorus in Infants and Children, Am. J. Dis. Child. **42**:749 (Oct., pt. 1) 1931.

19. Jeans, P. C., and Stearns, G.: The Effect of Vitamin D on Linear Growth in Infancy: II. The Effect of Intakes Above 1,800 U. S. P. Units daily, J. Pediat.

(Footnote continued on next page)

calcium-phosphorus ratios of retentions indicated an increased rate of skeletal development as compared with soft tissue development. During ingestion of plain fluid milk the children showed an average daily gain in recumbent length ranging from 0.018 to 0.024 cm. With the nonirradiated evaporated milk the gain was 0.012 to 0.016 cm., but with irradiated evaporated milk the rate of increase in length ranged from 0.024 to 0.032 cm. daily.

The effect of adding vitamin D is further illustrated by the data on acid-base balance. Both when plain fluid milk and when nonirradiated evaporated milk was given, the balances (base minus acid) ranged from -0.16 to $+0.20$ milliequivalent per kilogram per day, no trend being apparent with either type of milk. When the vitamin D intake was increased by irradiation of the evaporated milk, however, a resultant stabilization was shown by consistently positive base balances at a much higher level for all 3 children (0.24 to 0.44 milliequivalents per kilogram per day). These results emphasize the advantage of determining the total acid-base mineral balance rather than the balances of the three individual mineral elements (calcium, phosphorus and magnesium), as is often done.

The greatly enhanced storage of nitrogen when the children were given evaporated milk reflects a rapid synthesis of soft tissue. Further confirmation is found in the potassium-sodium ratios of the retentions, which were, respectively, 1.88, 2.28 and 1.23 during ingestion of plain fluid milk, 2.81, 3.14 and 1.45 when plain evaporated milk was substituted, and 2.70, 3.62 and 1.83 with the irradiated evaporated milk. The fact that the body contains somewhat less potassium, primarily a cellular constituent, than sodium, which is present largely in the extracellular fluids, lends credence to the belief that in these subjects the larger potassium-sodium retentions during ingestion of evaporated milk indicate that formation of soft tissue was progressing at a faster rate. The data obtained on the effect of evaporated milk on nitrogen and mineral metabolism in these average healthy children are in accordance with those obtained in studies with infants.[1b]

SUMMARY

The subjects of this metabolic study were adjusted to a rigidly controlled regime before initiation of the first experimental period. During the first period 400 Gm. of plain fluid milk was ingested daily by each child for twenty-five to forty consecutive days of metabolic study. During the twenty to twenty-five days immediately following, 400 Gm. of

13:730, 1938. Slyker, F.; Hamil, B. M.; Poole, M. W.; Cooley, T. B., and Macy, I. G.: Relationship Between Vitamin D Intake and Linear Growth in Infants, Proc. Soc. Exper. Biol. & Med. **37**:499, 1937.

dilute (1:1) evaporated milk was substituted for the fluid milk in each child's diet. For the next twenty-five days the only change in the dietary regimen was the addition of 90 U. S. P. units of vitamin D in irradiated evaporated milk.

An added impetus to formation of soft tissue resulted from the substitution of evaporated for fluid milk, as shown by the parallel increases in retention of nitrogen, sulfur and potassium, which were not accompanied by corresponding increases in retention of the other elements. When irradiated evaporated milk was included in the diet, the increased calcium-phosphorus ratios of the retentions, the higher levels and more consistent trends of the acid-base balances and the increase in rate of gain in recumbent length all indicated a more rapid and stable rate of formation of bone.

This study of 3 average healthy children 4½ to 6 years of age under favorable physical and mental environmental conditions during two hundred and forty-five experimental days emphasizes the necessity of determining all the acid-forming and base-forming elements and nitrogen, so that interpretations may be made with a recognition of the physiologic relationships existing in the utilization by the body of proportionate quantities of the elements involving changing rates of growth of soft tissue and skeletal structure.

HYPERPARATHYROIDISM IN CHILDREN

REPORT OF TWO CASES

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Hyperparathyroidism is due to hyperfunction of one or more parathyroid glands. Clinically it is characterized by muscular weakness, polyuria, pain in the bones and skeletal changes, which vary from slight kyphosis to marked shortening of stature and deformity of the extremities. Renal colic resulting from stones, diarrhea and loss of appetite may also be present. The fundamental roentgen change is decalcification, which may be merely uniform osteoporosis or may be associated with cysts in the medullary portion or below the periosteum. Frequently calcification is seen in the soft tissues. The ultimate criteria for diagnosis have been an increase of serum calcium and a decrease of serum phosphorus together with an increase in urinary excretion of calcium. The serum phosphatase activity is usually elevated.

The development of this concept of hyperparathyroidism is extremely interesting, particularly when one considers that it is the result of individual contributions of many clinicians and experimental workers over a mere quarter of a century.

In 1904 Askanazy [1] found a parathyroid tumor in a woman 51 years old who had a malacic condition of the bone resembling that described by von Recklinghausen and who during life had suffered many fractures. He failed to associate the conditions. Three years later Erdheim [2] went further with the study of his case and postulated a relation between the parathyroid hyperplasia and the osteomalacia, realizing that enlargement of the parathyroids occurs also in rickets. In 1925 Hoffheinz [3] collected 45 cases of hypertrophy or disease of the parathyroids, in 27 of which there were changes in the bones. Of these 27

From the Children's Memorial Hospital.

1. Askanazy, M.: Ueber Ostitis deformans ohne osteoides Gewebe, Arb. a. d. Geb. d. path. anat. Inst. zu Tübingen **4**:398, 1904.

2. Erdheim, J.: Ueber Epithelkörperbefunde bei Osteomalacie, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl. **116**:311, 1907.

3. Hoffheinz, S.: Ueber Vergrösserungen der Epithelkörperchen bei Ostitis fibrosa und verwandten Krankheitsbildern, Virchows Arch. f. path. Anat. **256**:705, 1925.

cases, 17 were instances of osteitis fibrosa cystica, 7 of osteomalacia and 2 of rickets. About the same time Berman,[4] Hanson[5] and Collip,[6] working independently, isolated the active principle of the parathyroids and produced hypercalcemia in normal and parathyroprivic animals. Greenwald and Gross[7] and Albright and associates[8] further demonstrated that such administration of parathyroid extract was followed by increased excretion of calcium in the urine. Later Albright and Ellsworth[9] found that the first effect of injection of parathyroid extract was not hypercalcemia but hypophosphatemia. The final proof of the relation of parathyroid glands to osteitis fibrosa cystica came in the production of characteristic changes of the bone in experimental animals by injection of parathyroid extract. This was accomplished about the same time by Johnson[10] and by Jaffe, Bodansky and Blair.[11]

The first case of improvement as a result of removal of an adenoma of the parathyroid was reported by Mandl[12] in 1926. Since that time about 150 cases of primary hyperparathyroidism have been reported,

4. Berman, L.: A Crystalline Substance from the Parathyroid Gland That Influences the Calcium Content of the Blood, Proc. Soc. Exper. Biol. & Med. **21**: 465, 1924.

5. Hanson, A. M.: Elementary Chemical Study of the Parathyroid Glands of Cattle, Mil. Surgeon **52**:280, 1923.

6. Collip, J. B.: Extraction of Parathyroid Hormone Which Will Prevent or Control Parathyroid Tetany and Which Regulates the Level of Blood Calcium, J. Biol. Chem. **63**:395, 1925.

7. Greenwald, I., and Gross, J.: Effect of Thyroparathyroidectomy in Dogs upon Excretion of Calcium, Phosphorus and Magnesium, J. Biol. Chem. **66**:185, 1925.

8. Albright, F.; Bauer, W.; Ropes, J., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: Effect of Parathyroid Hormone, J. Clin. Investigation **7**:139, 1929.

9. Albright, F., and Ellsworth, R.: Studies on the Physiology and the Parathyroid Glands: I. Calcium and Phosphorus Studies on a Case of Idiopathic Hyperparathyroidism, J. Clin. Investigation **7**:183, 1929.

10. Johnson, J. L.: (*a*) Experimental Chronic Hyperparathyroidism, Chicago, University of Chicago Press, 1930; (*b*) Experimental Chronic Hyperparathyroidism: II. Osteitis Fibrosa Produced in Rats, Am. J. M. Sc. **183**:761, 1932; III. Osteitis Fibrosa Produced in Puppies, ibid. **183**:769, 1932; IV. Effects of Administration of Irradiated Ergosterol, ibid. **183**:776, 1932.

11. Jaffe, H. L., and Bodansky, A.: Experimental Fibrous Osteodystrophy (Ostitis Fibrosa) in Hyperparathyroid Dogs, J. Exper. Med. **52**:669, 1930. Jaffe, H. L.; Bodansky, A., and Blair, J. E.: Fibrous Osteodystrophy (Osteitis Fibrosa) in Experimental Hyperparathyroidism of Guinea-Pigs, Arch. Path. **11**:207 (Feb.) 1931; Erzeugung von Ostitis fibrosa (Osteodystrophia fibrosa) durch Epithelkörperchen-Extrakt, Klin. Wchnschr. **9**:1717, 1930.

12. Mandl, F.: Attempt to Treat Generalized Fibrous Osteitis by Extirpation of Parathyroid Tumor. Zentralbl. f. Chir. **53**:260. 1926.

in 12 of which [13] involvement began during childhood. In all of these except 3 an adenoma of the parathyroid was removed; in 1 of the remaining cases an exploratory operation on the neck was performed, and parathyroid tissue was removed, but no adenoma was found (table 1).

REPORT OF CASES

CASE 1.—E. B., a girl 11 years of age, was admitted to the Children's Memorial Hospital on Aug. 23, 1932. Her disability began fourteen months previously, on June 8, 1931, when she fell while at school, sustaining two fractures of the right humerus. Six weeks later she had an illness characterized by fever, convulsions and vomiting. This lasted for two weeks, after which she had difficulty in walking, needle pains along the bones of all the extremities, worse at night, pain in the back and polyuria.

The birth and development were normal. Cod liver oil was given regularly during infancy. Three siblings were living, while five had died in infancy of undiagnosed illnesses.

Hyperparathyroidism was suspected, but this diagnosis was not yet confirmed. The mother could not part with this child, her youngest, even for a brief hospitalization. Two months later, on Oct. 21, 1932, because of progressive emaciation, the girl was brought back to the hospital. Her weight had dropped from 73 to 47 pounds (33.1 to 21.3 Kg.). She complained of intense pain in her fingers but was apparently able to walk with less discomfort than when first seen.

Physical examination revealed a greatly emaciated, intelligent girl with generalized muscular weakness and atrophy. The joints appeared prominent because of the wasting, but the right knee was definitely larger than the left. Tenderness could be elicited with slight pressure over the hamstring muscles and the carpal-metacarpal joints on the right. The only other significant finding was an abscessed tooth, which proved to have a cyst at the root.

A roentgen examination (fig. 1) at this time revealed: (1) generalized osteoporosis, (2) changes in contour of the long bones (slender shafts with relative enlargement of the epiphyses), (3) normal appearance of skull bones (two years

13. (*a*) Pemberton, J. de J., and Geddie, K. B.: Hyperparathyroidism, Ann. Surg. **92**:202, 1930. (*b*) Cooley, T. B.: Hyperparathyroidism and Similar Diseases of Bone, Tr. Am. Pediat. Soc. **43**:20, 1931. (*c*) Cosin, C. F.: Hyperparathyroidism: A Case of Osteitis Fibrosa Cystica with Cystic Adenoma, Guy's Hosp. Rep. **81**:297, 1931. (*d*) Landon, J. F.: Parathyroidectomy in Generalized Osteitis Fibrosa Cystica, J. Pediat. **1**:544, 1932. (*e*) Dyke, S. C.; Walker, R. M., and Freeman, E.: Adenoma of Parathyroid Associated with Generalized Osteitis Fibrosa, Lancet **2**:530, 1933. (*f*) Dresser, R.: Osteitis Fibrosa Cystica Associated with Parathyroid Overactivity, Am. J. Roentgenol. **30**:596, 1933. (*g*) Boyd, J. D.; Milgram, J. E., and Stearns, G.: Clinical Hyperparathyroidism, J. A. M. A. **93**: 684 (Aug. 31) 1929. (*h*) Churchill, E. D., and Cope, O.: Parathyroid Tumors Associated with Hyperparathyroidism, Surg., Gynec. & Obst. **58**:255, 1934. (*i*) Duken, J.: Beitrag zur Kenntnis der malacischen Erkrankungen des kindlichen Skelettsystems: Spätrachitis und Osteodystrophia fibrosa, Ztschr. f. Kinderh. **46**: 114, 1928. (*j*) Albright, F.; Aub, J. C., and Bauer, W.: Hyperparathyroidism: A Common and Polymorphic Condition as Illustrated by Seventeen Proved Cases from One Clinic, J. A. M. A. **102**:1276 (April 21) 1934.

TABLE 1.—*Hyperparathyroidism in Children*

Author	Age.	Sex	Onset	Changes of Bone	Renal Calculi	Adenoma Removed	Preoperative Blood Chemistry, Mg./100 Cc.	
							Calcium	Phosphorus
Pemberton and Geddie [13a]	14 yr.	F	12½ yr.	Osteoporosis (including skull)		Yes	15.5	3.2
Cooley [13b]	14 yr.	F	10½ yr.	Osteitis fibrosa cystica (including skull)		Yes	13.6	2.6
Cosin [13c]	17 yr.	M	14 yr.	Osteitis fibrosa cystica	Bilateral	Yes	16.5	2.1
Landon [13d]	2½ yr.	M	6 mo.	Osteitis fibrosa cystica		No	10.5	3.0
Dyke, Walker and Freeman [13e]	14 yr.	F	10 yr.				19.4	5.5
Dyke, Walker and Freeman [13e]	14 yr.	F	12 yr.	Osteitis fibrosa cystica		Yes	13.6	2.8
Dresser [13f]	15 yr.	M	12 yr.	Osteoporosis		Yes	16.7	
Boyd, Milgram and Stearns [13g]	10 yr.	M	9 yr.	Osteoporosis epulis, thin skull		Yes	19.4	4.0
Churchill and Cope [13h]	13 yr.	F	9 yr.	Osteitis fibrosa cystica		Yes		
Albright, Aub and Bauer [13j]	13 yr.	M	9 yr.	Osteitis fibrosa cystica (giant cell tumors)		Yes	12.5	4.7
Duken [13i]	7 yr.	F	6 yr.	Osteitis fibrosa cystica; renal rickets	Yes	Yes	12.1	4.7
Duken [13i]	14 yr.	F	13 yr.	Osteodystrophia fibrosa (like late rickets)		No	14	5
						No	15.8	
Anspach and Clifton							18	2.5
Case 1	11 yr.	F	9½ yr.	Osteoporosis		Yes	16.5	2.5
Case 2	11 mo.	F	3 mo.	Rickets-like osteoporosis, thinning of skull		Roentgen therapy	16.2	2.3

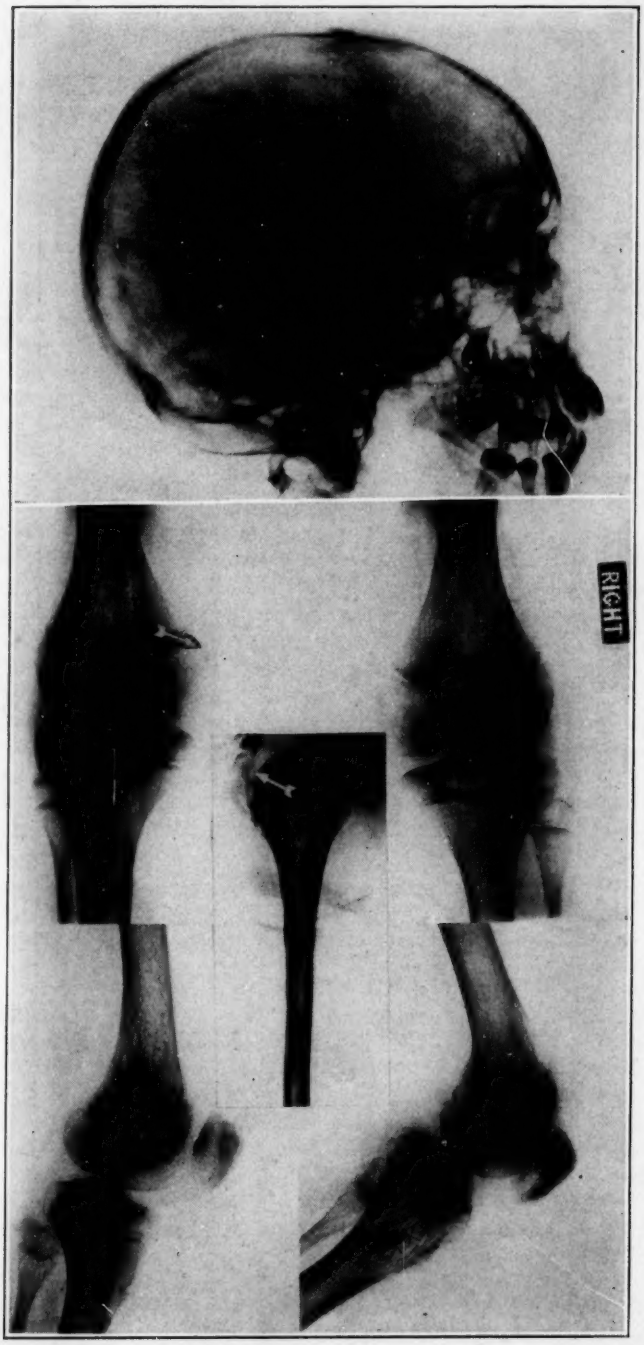

Fig. 1 (case 1).—E. B. at the age of 11 years. Note the osteoporosis, enlargement of epiphyses at the joints and calcification (arrows) in the tendons of the knee and in the region of the acromion bursa. Bones of the skull do not show appreciable change, but two years later granular osteoporosis was evident.[14]

later there was marked granular osteoporosis[14]) and (4) calcification in the tendon at the mesial aspect of the right knee and in the bursa of the right acromion.

The blood contained 70 per cent hemoglobin (Sahli); there were 4,900,000 erythrocytes and 13,800 leukocytes per cubic millimeter; the differential count was normal. The urine was alkaline; it contained a trace of albumin and a large amount of triple phosphates. The serum calcium level was 16.2 mg. and the phosphorus 2.2 mg. per hundred cubic centimeters. Tuberculin and Wassermann reactions were negative. Renal function was normal.

A diagnosis of hyperparathyroidism was made, and parathyroidectomy was advised. The operation was refused, but the child was permitted to remain in the hospital six months. Table 2 shows the persistence of hypercalcemia and hypophosphatemia during this period of observation.

Major convulsions began in March 1933, nearly two years after the febrile illness previously described. Whereas the patient had been doing satisfactory work in the fifth grade at school, it soon became apparent that she had progressive mental deterioration. At this time a roentgenogram showed granular osteoporosis of the skull table,[14] not present at the first examination, six months previously; in addition, calcification of the acromion bursa was found to be increased.

TABLE 2.—*Serum Calcium and Phosphorus Values of E. B. Before Operation*

Date	Calcium, Mg./100 Cc.	Phosphorus, Mg./100 Cc.
10-27-31	16.5	2.5
11- 1-32	15.1	2.6
11-30-32	16.6	2.2
1-25-33	15.5	2.7
2- 4-33	14.1	2.5
2-15-33	13.7	2.7
3- 1-33	14.0	2.5

In March 1935, when the patient was 13½ years old, she was again brought to the outpatient department of the Children's Memorial Hospital, because the convulsions had become more frequent and the weakness had progressed to the stage of rendering her helpless. At this time the parents were willing to permit surgical intervention, and the patient was transferred to the University of Chicago Clinics. On March 16 Dr. Phemister removed a parathyroid tumor from the right lower pole of the thyroid.

After operation the patient's condition improved so that she was free from pain; she regained her strength so that she could walk and was able to dress herself. The convulsions, however, continued and could be controlled only partially by sedatives. The serum calcium and phosphorus values returned to normal within twenty-four hours after operation.

On Sept. 21, 1938, the parents brought the patient, now 17 years of age, to the dispensary in response to the request for a check-up examination (fig. 2). They stated that she had remained ambulatory for eighteen months after the operation; then, because of increased frequency of convulsions, she had become bedridden. She presented the picture of a mental defective, with marked muscular atrophy and contractures. She had no clinical or laboratory evidence of recurrence of hyperparathyroidism.

14. Hodges, P. C.: Skeletal Changes in Disturbances of the Parathyroid Glands, Radiology **26**:663, 1936.

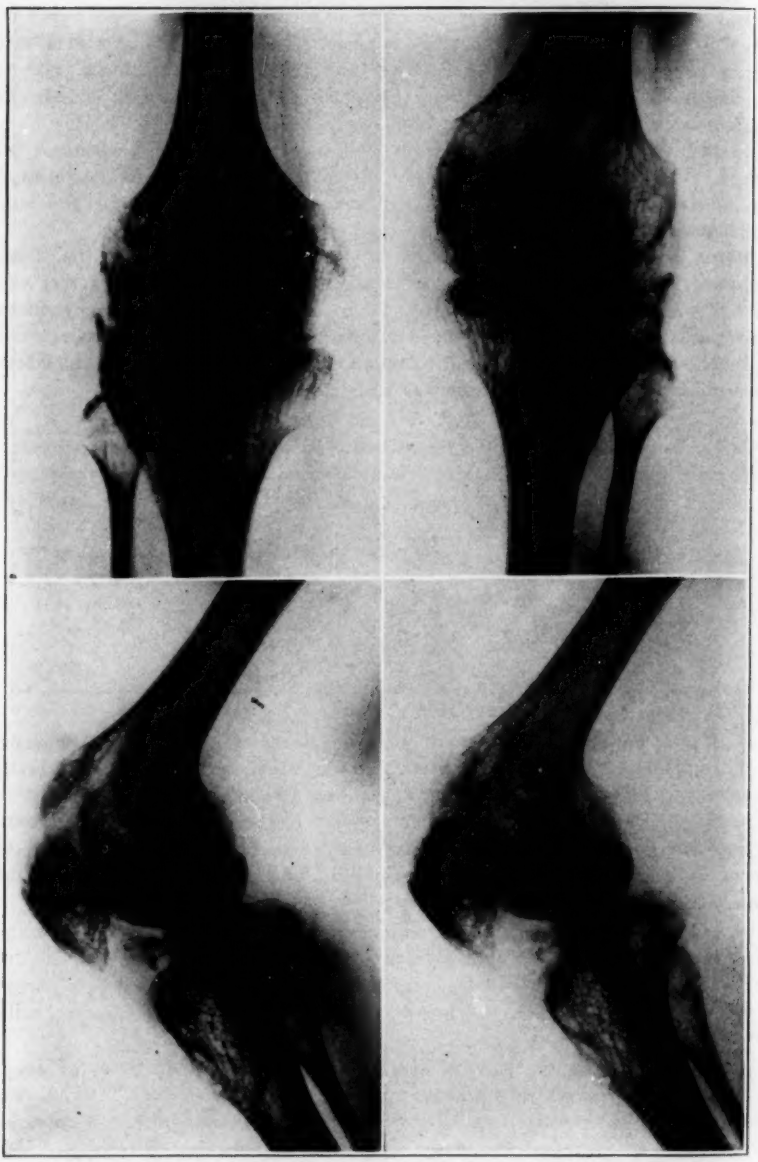

Fig. 2.—E. B. at the age of 17 years. Calcification between the condyles is evident. The epiphyses are still large.

CASE 2.—J. B., born Aug. 15, 1934, is 4 years old at the time of writing. It is significant that she had a normal birth and that by the third month her weight had doubled. When she was 6 days old feedings of lactic acid, evaporated milk and dextrimaltose were started. Cod liver oil was first given at the age of 1 month; the dose was increased to 2 drachms (7.4 cc.) daily by the second month. Orange juice was then added, administration being continued without interruption.

When 3 months old the baby began to lose her appetite and failed to gain weight. By the fourth month there was marked polyuria, and the mother noticed tenderness of the extremities, especially when she picked the baby up by the arms. Dr. F. W. Griffith,[15] the family physician at this time, described tender swellings in the region of the joints, visible bulging of the anterior fontanel and crepitation in the occipital region. The bulging of the fontanel increased, but there were no other clinical signs of increased intracranial pressure. Roentgen examination of the whole body at the age of 9 months revealed an unusual type of "cupping" at the ends of the shafts of all long bones. Through the zones of provisional cartilage formation, ossification was evident only as thin longitudinal streaks of coarse trabeculae in the larger bones and as markedly thinned cortex in the smaller bones (fig. 3). The anterior fontanel was larger than normal, and the membranous bones curved upward at its borders (fig. 8*A*). The digitations of the skull were marked, the skull tables were thin, and many fracture lines were evident in the postparietal region adjacent to the lambdoidal suture. The sutures were not abnormally separated. When the baby was 11 months old she was admitted to Dr. Joseph Brennemann's service at the Children's Memorial Hospital for further study. Her clinical condition, characterized by anorexia, polyuria, hypotonia and skeletal changes, revealed by the roentgenograms, suggested hyperparathyroidism or renal rickets.

Physical examination revealed a poorly nourished and underdeveloped baby who cried when moved. She weighed only 13 pounds (5,897 Gm). The anterior fontanel measured 4 by 4 cm. and bulged nearly 2 cm. The sagittal suture was elevated, forming a ridge which terminated in a small posterior fontanel. This midline elevation continued forward on the frontal bone. The central incisors had erupted, and there were no abnormalities of the gums. Tender epiphysial swellings were present, particularly at the wrists and ankles. The costochondral junctions were enlarged, suggesting rickets.

The blood showed moderate secondary anemia. The hemoglobin content was 78 per cent (Sahli); erythrocytes numbered 4,900,000 and leukocytes 11,800; the differential count was normal. The serum calcium level was elevated to 16.2 mg. per hundred cubic centimeters and the phosphorus level decreased to 2.3 mg. Tests showed normal renal function, but there was some elevation of the nonprotein nitrogen value (42.1 mg. per hundred cubic centimeters). Because of the age of the patient, we were unsuccessful in efforts to collect twenty-four hour specimens of urine for determination of total calcium excretion. The urinalysis was normal except for a large amount of triple phosphates.

While the baby was in the hospital, it was impossible to get her to take as much food as when at home. She lost 1 pound (454 Gm.) during five days of observation.

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15. Dr. F. W. Griffith referred the patient and made further observation of this case possible. The Sherman Hospital, Elgin, Ill., furnished frequent roentgenograms and roentgen therapy.

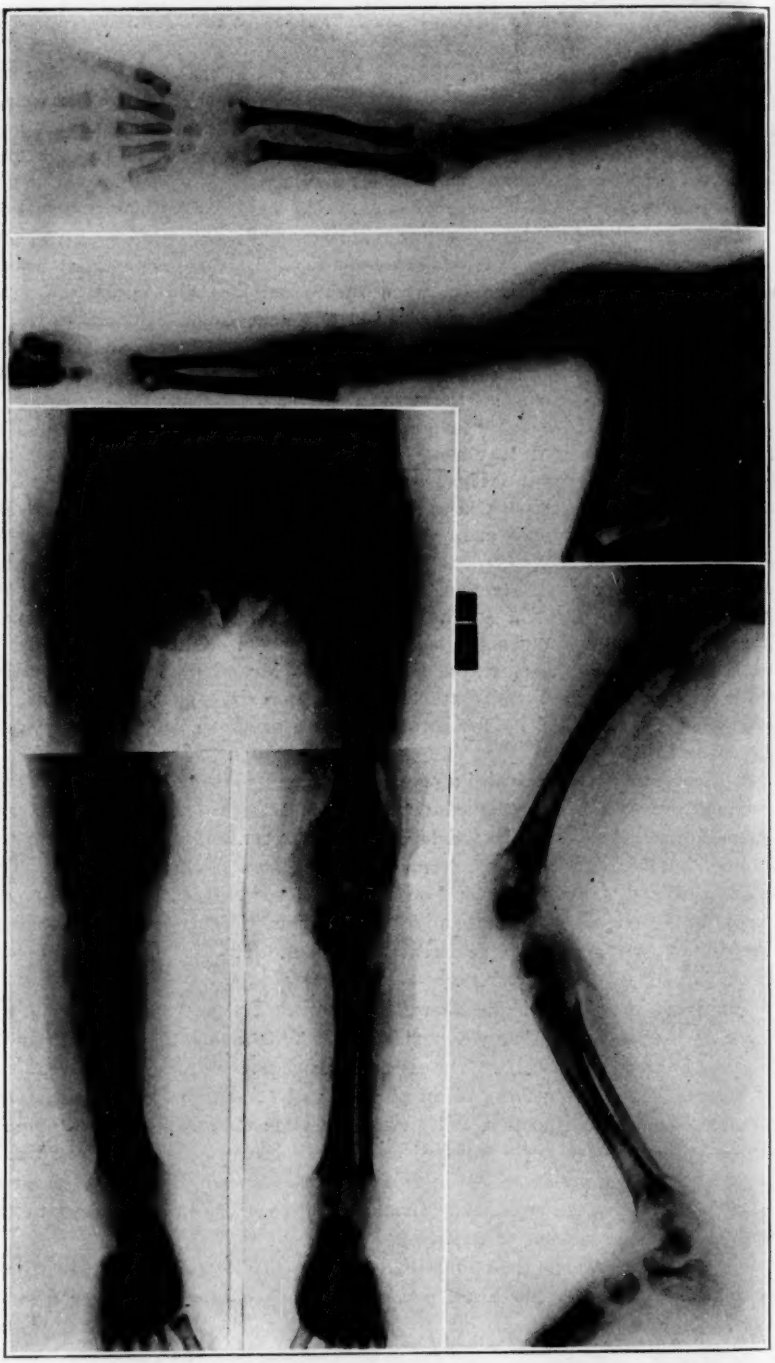

Fig. 3 (case 2).—J. B.'s extremities at the age of 9 months. Note the absence of calcification and the presence of unusual cupping at the ends of the shafts, where longitudinal columns of coarse trabeculae and markedly thinned cortex are seen. In the larger bones a scalloped appearance is produced.

The parents were told the clinical diagnosis of hyperparathyroidism, and operation for removal of a possible parathyroid tumor was advised. This they refused, and the child was removed from the hospital.

On July 25, 1936, after another year at home, the child was brought back to the hospital. Her condition had grown worse in every way. At the age of 2 years she weighed only 15 pounds (6,804 Gm.). Her appetite was still capricious, and milk constituted the main food. Muscular weakness was marked. The child

Fig. 4.—J. B. at the age of 2 years and 3 months. There is marked bulging of the anterior fontanel. Note the "pithed frog" appearance and enlargement at the wrists.

could sit up about one hour a day but made no effort to stand. The mother thought that since May 1936 the child could not see well. Dentition and talking had progressed normally. The patient's general appearance suggested marked malnutrition and underdevelopment (fig. 4). Veins over the forehead were prominent; the eyes were prominent, and there was lateral nystagmus. The entire head felt soft and nodular, especially at the sides. The blunt, cone-shaped bulging of the anterior fontanel, previously described, was even more exaggerated, and the margins

Fig. 5.—J. B.'s extremities at the age of 2½ years. The subepiphysial zones are now almost devoid of calcification and are markedly enlarged. The bones have increased only slightly in length. The growth of the ossified portion of the shaft has been practically nil for more than a year. Osteoporosis of all bones has reached a high point.

of the membranous bones extended possibly higher than previously. The suture lines were elevated. The optic disks were pale. The enlargement at the ends of the long bones was more marked than the year before. Motion of the spine seemed to cause pain.

Roentgenograms made at this time showed marked increase in the loss of osseous density as compared with that noted at previous examinations. The zones of provisional cartilage of the long bones were enlarged and devoid of evidence

Fig. 6.—J. B.'s extremities at the age of 4 years, ten months after conclusion of a course of roentgen therapy of the neck. Marked recalcification has occurred. Only a slight deficiency of calcification remains in the subepiphysial zones. The serum calcium level is normal, and physically the patient is markedly improved.

of calcification, except for sparse, longitudinal, coarsely trabeculated columns of thinned cortex which extended from the ossified central portion of the shaft toward the epiphysis (fig. 5). The thin skull tables were markedly osteoporotic, showing only a minimum of calcification (fig. 8 *B*). The base of the skull appeared to be invaginated, apparently owing to weakened support in the region of the atlas.

Chemical studies showed persistence of the hypercalcemia but no hypophosphatemia; the value for calcium was 14.5 mg., for phosphorus 3.7 mg. and for phosphatase 12 Bodansky units. The only evidence of renal damage was elevation of the nonprotein nitrogen content to 48.9 mg. per hundred cubic centimeters.

At this time the parents still refused operation but consented to high voltage roentgen therapy over the neck. Ten treatments, of 184 roentgens each, were given

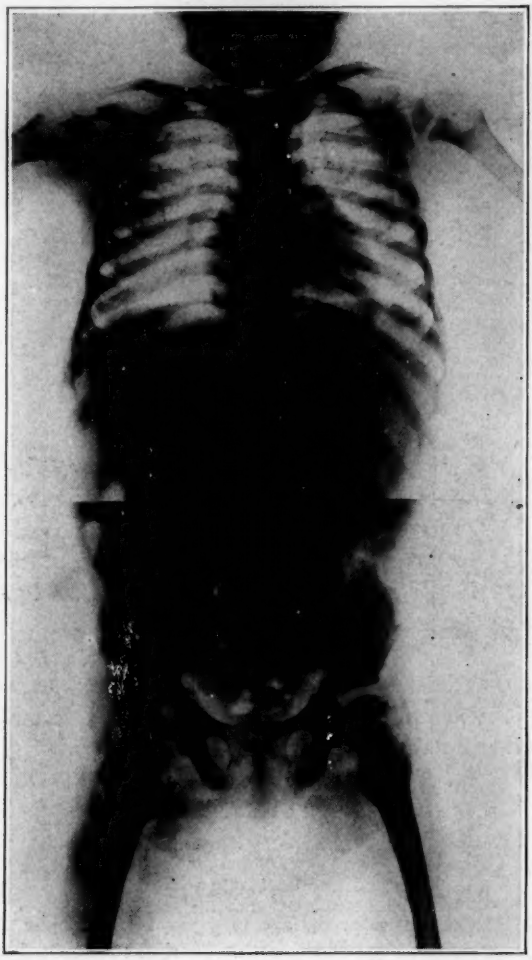

Fig. 7.—Roentgenogram of J. B. Note the flaring at the ends of the ribs and moderate scoliosis.

at weekly intervals. On November 24, one month after the last treatment, the child was again admitted for observation. The mother had noticed some definite changes: for example, improvement in appetite, remissions of polyuria lasting about one week of each month and complete relief of constipation. The patient's

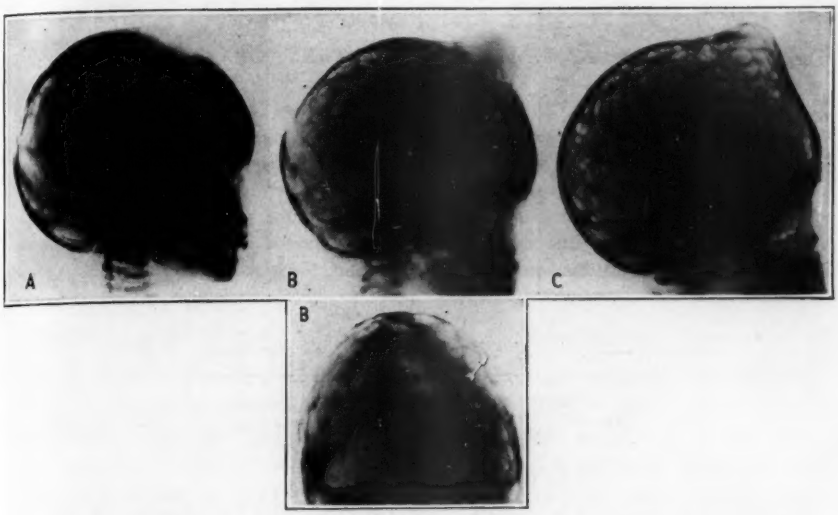

Fig. 8.—Roentgenograms of the skull of J. B. at the age of *A*, 9 months; *B*, 21 months, and *C*, 4 years, showing the bulging fontanel and increased digitations. There was progressive decalcification before roentgen therapy, then rapid calcification occurred, possibly with premature closure of the sutures. Note marked osteoporosis at 21 months, just before roentgen therapy (arrow).

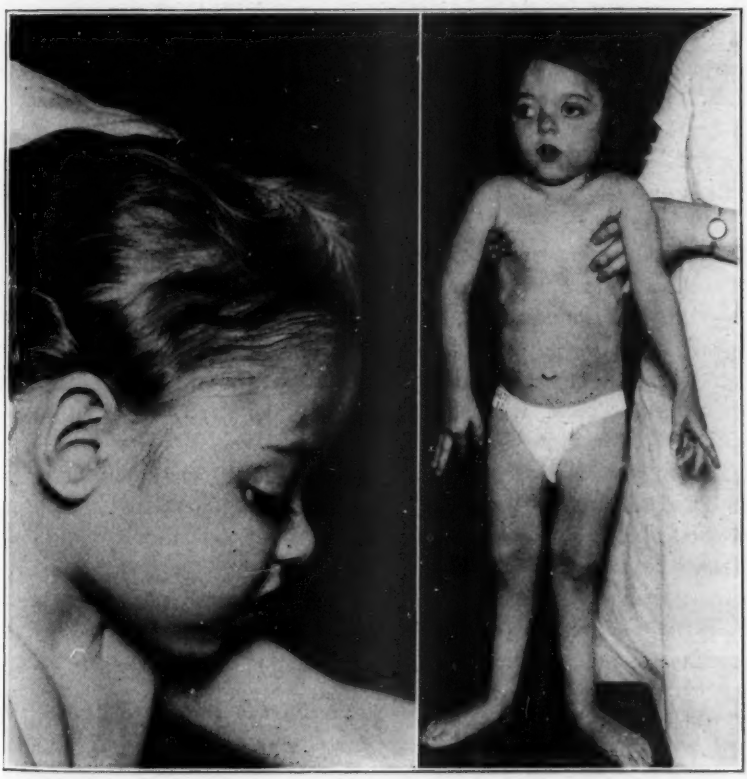

Fig. 9.—J. B. at the age of 4 years. There is marked improvement in nutrition and muscle tone, but bulging of the fontanel persists. Genu valgum is apparently due to soft endochondral bone, as the patient attempts to stand or walk.

vision, poor in July, had continued to fail, until by November she was blind. Although there was some evidence of arrest of hyperparathyroidism, she still had hypercalcemia. The serum phosphorus level was well within normal limits.

By June 1938 there was marked physical improvement, and roentgenograms showed almost complete recalcification of the bones (figs. 6, 7, 8 *C* and 9). At this time the calcium value was normal and the phosphorus value elevated, and there was a positive calcium balance. Table 3 gives the comparative values for a period of three years.

TABLE 3.—*Results of Chemical Studies of the Blood of J. B.*

Date	Age of Patient	Calcium, Mg./100 Cc.	Phosphorus, Mg./100 Cc.	Phosphatase, Bodansky Units	Nonprotein Nitrogen Mg./100 Cc.	Cholesterol, Mg./100 Cc.
7/30/35	11½ mo.	16.2	2.3		42.1	241
7/24/36	23 mo.	14.5	3.7	12	48.9	
11/24/36	27 mo.	14.9	4.38	2	48.9	243
6/20/38	4 yr.	11.7	5.85	1.5		

COMMENT

Diagnostic criteria for hyperparathyroidism have been based largely on clinical studies of adults, with animal experimentation for corroboration. Primary hyperparathyroidism has been considered due to adenoma or to idiopathic generalized parathyroid hyperplasia, while secondary hyperparathyroidism has been seen principally as associated with renal insufficiency. Parathyroid enlargement secondary to severe rickets has also been known to occur. Hypercalcemia and hypophosphatemia were recently observed at this institution in a case of lymphosarcoma. Hypercalcemia also is associated with certain other neoplasms of bone, notably multiple myeloma.

Primary hyperparathyroidism has been divided into the following types:[16] (1) the classic form, in which the typical skeletal changes of osteitis fibrosa cystica predominate; (2) the osteoporotic form, in which decalcification of the skeleton is generalized and there is no tendency to cyst formation, and (3) the metastatic type, in which the chief symptoms are associated with deposition of calcium in the soft tissues, especially in the kidneys.

The first case here reported exemplifies the changes seen in both adults and children of the older age group, i. e., generalized osteoporosis and metastatic calcification in the soft tissues of the right shoulder and knee.

In case 2 there were clinical signs of primary hyperparathyroidism rather than of renal rickets or vitamin D deficiency, namely, hypercalcemia, hypophosphatemia, slight increase in serum phosphatase, good

16. Shelling, D. H.: Parathyroids in Health and Disease, St. Louis, C. V. Mosby Company, 1935, p. 179.

renal function and a history of adequate intake of vitamin D. There was more evidence of acalcification in this case than in any previously reported. We believe that this degree of acalcification is representative of a form of hyperparathyroidism in a period of active growth.

It has been held by Jaffe, Bodansky and Blair that deposition and resorption of bone occur throughout the skeleton but are more rapid in regions of active growth. This would explain the severe grade of changes found in our patient, which in the roentgenograms appear as marked generalized decalcification and acalcification at the epiphysial cartilages in the long bones, particularly noticeable at the ends of the femurs and at the proximal ends of the tibias.

Not only because of the very young age of the second patient would one expect the severe symptoms but because of the high calcium diet. (It will be recalled that her principal food was milk.) The adverse influence of a high calcium diet is thought to be due to its accentuation of the hypercalcemic state of the body fluids. The anorexia present defeated all attempts to introduce an adequate variety of foods into the diet.

Roentgen therapy over the neck apparently was a satisfactory means of controlling the hyperactivity of the parathyroids. Merritt [17] seems to have been the first to irradiate with roentgen rays a patient who had hyperparathyroidism. After irradiation directed toward the bone, cystic areas rapidly recalcified. Landon later noted similar results in a child 2½ years old. We were encouraged to try roentgen therapy of the neck because of failing repeatedly to get permission for exploration for a possible tumor and also because the decalcification and relative acalcification increased to an alarming degree as time went on. Recalcification of the bones and clinical improvement of the patient promptly followed roentgen therapy (figs. 7 and 8). The fontanel continued to bulge but was rapidly enclosed by ossification of the membranous bones. All bones became more dense, and the cupping at the ends of the shafts of the long bones, seen previously in roentgenograms, rapidly disappeared. Our latest observation revealed that recalcification was occurring rapidly but was still slightly incomplete. That these zones of recent calcification were still less resistant than is normal was suggested by recent distortion, or slight tipping, of the epiphysis, which resembles somewhat the changes seen in so-called late or renal rickets. The pacchionian depressions were still present to a remarkable degree, showing more clearly because of recalcification, and the suture lines could not be made out, which suggests possible premature closure (fig. 8 *C*).

17. Merritt, E. A., and Lattman, I.: X-Ray Treatment in Hyperparathyroidism, Radiology **26**:673, 1936.

Chown [18] has presented 3 unusually interesting patients having delayed senescence of cartilage at the ends of the shafts of the long bones, the roentgen appearance somewhat simulating that in our case 2. He attributed the disturbance to pituitary disease. In 2 of his cases, in which the patient succumbed early in life, the clinical changes in the blood were minimal or normal and there was marked loss in kidney function, the picture varying greatly from that in our case.

Deformities and disabilities can be relieved only partially by control of the disease. Pain and polyuria have been relieved, but at the time of writing the distortion of the calvarium and the blindness have not been altered.

There is some evidence of progressive renal impairment. This was first reflected early in the disease by elevation of the nonprotein nitrogen value, which has persisted. Now there is also elevation of the serum phosphorus level, and the urine shows a few granular casts.

SUMMARY AND CONCLUSIONS

The cases of 2 children of different ages with hyperparathyroidism are presented.

The first case, that of a girl 9 years old at the onset of symptoms, exemplifies the changes seen in adults and older children, i. e., generalized osteoporosis and metastatic calcification in the soft tissues of the right shoulder and the knees. Removal of a parathyroid adenoma relieved the condition, and there was no recurrence of hyperparathyroidism during the subsequent three years.

The second case is that of an infant whose symptoms were first noted at the age of 3 months and progressed for two years. Skeletal deformities and muscular weakness were most severe. Blindness, thought to be due to increased intracranial pressure secondary to distortion and fractures of a soft skull, developed during the second year. Because of the hypercalcemia and hypophosphatemia, together with initial normal renal function, we believe this is a case of primary hyperparathyroidism, despite skeletal changes somewhat resembling those of renal rickets. The persistent loss of density of the endochondral zones noted on roentgenograms, we believe, indicates that acalcification as well as decalcification may be a feature of primary hyperparathyroidism during active body growth.

During the period of observation prior to treatment, while there were persistent hypercalcemia and increasing decalcification, the serum phosphorus value returned to normal.

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18. Chown, B.: Renal Rickets and Dwarfism: A Pituitary Disease, Brit. J. Surg. **23**:552, 1936. Chown, B., and Lee, M.: Renal Rickets and Dwarfism as a Pituitary Disease, Am. J. Dis. Child. **53**:117 (Jan., pt. 1) 1937.

After roentgen irradiation of the neck, the bones recalcified. Polyuria and hypotonia were relieved. During the two years following irradiation of the neck there was no evidence of dysfunction of the parathyroids. This is the youngest patient reported on thus far and the only one we know of who showed spectacular recalcification following roentgen therapy of the parathyroids.

Miss Mary Corbin, of Children's Memorial Hospital, Dr. Smith Freeman, of Northwestern University Medical School, and Dr. Walter Highman, of the University of Chicago Clinics, gave assistance in the chemical studies.

707 Fullerton Avenue.

Case Reports

JEJUNAL INTUSSUSCEPTION OF THE NEWBORN

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Intestinal obstruction is unusual in the neonatal period, occurring in 1 of every 20,000 newborn infants, according to Tow.[1] However, Cruickshank [2] found at postmortem examination that 3 of a series of 800 neonatal deaths (between birth and the fourth week) were due primarily to obstruction of the large bowel. These intestinal obstructions may be caused by congenital occlusion by developmental bands or membranous outgrowths, a tumor of the intestinal wall or its contiguous structures, the formation of a mucous plug, volvulus or intussusception. Of these possible causes of intestinal obstruction, one of the most unusual is intussusception. Hunter [3] in 1789 discussed the surgical pathology of intussusception. Hutchinson,[4] in his report of successful operative treatment for intussusception in 1874, stated that the first successful operation was reported in 1784.[5] However, Ashhurst [6] declared that the first successful operative reduction of intussusception was reported in 1672 by Barbette.[7] Fitzwilliam,[8] in a sum-

From the Wyandotte General Hospital.

1. Tow, A.: Diseases of the Newborn, New York, Oxford University Press, 1937, p. 20.

2. Cruickshank, J. N.: Child Life Investigations: The Causes of Neo-Natal Death, Medical Research Council, Special Report Series, no. 145, London, His Majesty's Stationery Office, 1930.

3. Hunter, J.: On Introsusception, Tr. Soc. Improve. M. & Chir. Knowl., London **1**:103-108, 1793.

4. Hutchinson, J.: A Successful Case of Abdominal Section for Intussusception, Med.-Chir. Tr., London **57**:31-75, 1874.

5. Hévin, M.: Recherches historiques sur la gastrotomie, ou l'ouverture du bas-ventre, dans le cas du volvulus ou d'intussusception d'un intestin, Mém. Acad. roy. de chir. **4**:201-242, 1784.

6. Ashhurst, J.: On Laparotomy or Abdominal Section as a Remedy for Intussusception, with Tables Showing the Results of the Operation in Cases of This Affection, Am. J. M. Sc. **68**:48-64, 1874.

7. Barbette, P.: An non etiam praestaret, facta diffectione muscusorum & peritonae, digitis susceptum intestinum extrahere, quam morti aegrotantem committere? in Opera chirurgico-anattomica, Lugd. Bat., J. à Gelder, 1672; cited by Ashhurst.[6]

8. Fitzwilliam, D. S. C.: The Pathology and Etiology of Intussusception from the Study of One Thousand Cases, Lancet **1**:628-633 and 709-713, 1908.

mary of 1,000 cases of intussusception, largely taken from the literature, reported only 1 occurring in the first month of life. Helmholz,[9] on the other hand, in a report of 2 cases of intestinal obstruction occurring in infants during the first month of life, reviewed 12 other cases and found that in 3 of the 14 the condition was caused by intussusception.

Chiari [10] was the first to report intussusception in the neonatal period. Hess [11] compiled a series of 1,028 cases of intussusception, in only 8 of which the patients were under 3 months of age. The 2 youngest were not operated on and died at 6 days of age. Tweedy [12] reported intussusception in an infant 2 days old. The outstanding symptom was marked melena, and death occurred on the third day post partum. Diagnosis in these last cases was established by postmortem examination.

Dowd [13] reported the first successful treatment of intussusception in the neonatal period. The patient, a boy aged 5 days and weighing 6½ pounds (2,948 Gm.), operated on under ether anesthesia, had one third of the colon resected for irreducible intussusception. The symptoms of paroxysmal pain associated with blood in the stools had their onset thirty-seven hours prior to operation. Abdominal and rectal examination revealed a palpable mass in the right lower quadrant 1½ by 4½ inches (3.8 by 11.4 cm.). Perrin and Lindsay [14] observed intussusception in an infant followed by death in one day. Peterson [15] reported the case of a child 6 days old.

Gelston and Sappington [16] made the first report which included details of a complete autopsy after intussusception in the neonatal period. Schiavone [17] reported occurrence in a 9 day old infant. Mora and Aries [18]

9. Helmholz, H. F.: Two Cases of Atresia of the Small Intestine, Bull. Johns Hopkins Hosp. **18**:370-375 (Sept.) 1907.

10. Chiari, H.: Zur Entstehung der congenitalen Dermatresie aus Intussusception, Prag. med. Wchnschr. **27**:267-269 (May 28) 1903.

11. Hess, J. H.: Intussusception in Infancy and Childhood with Collection of 1,028 Cases with Statistics, Arch. Pediat. **22**:655-683 (Sept.) 1905.

12. Tweedy, E. H.: Intussusception, Brit. M. J. **1**:1402, 1906.

13. Dowd, C. N.: Resection of One-Third of the Colon for Irreducible Intussusception in an Infant Five Days Old, Ann. Surg. **57**:713-717 (May) 1913.

14. Perrin, W. S., and Lindsay, E. C.: Intussusception: A Monograph Based on Four Hundred Cases, Brit. J. Surg. **9**:46-71 (July) 1921.

15. Peterson, E. W.: Acute Intestinal Obstruction in Infancy and Childhood, Surg., Gynec. & Obst. **35**:436-439 (Oct.) 1922.

16. Gelston, C. F., and Sappington, S. E.: Acute Intussusception in Newborn with Report of Case Including Autopsy Findings, Arch. Pediat. **47**:185-189 (March) 1930.

17. Schiavone, G. A.: Invaginación intestinal en el lactante: A propósito de una observación clínica en un lactante de 9 días, Semana méd. **1**:687-696 (Feb. 27) 1936.

18. Mora, J. M., and Aries, L. J.: Acute Intussusception in Early Weeks of Life, Am. J. Surg. **32**:176-177 (April) 1936.

recorded the case of a 27 day old boy. Steele [19] operated on and successfully reduced a massive invagination in an infant 4 days old, although death occurred the next day. Postmortem examination disclosed free blood in the peritoneal cavity but no recurrence of the intussusception or evidence of peritonitis. Mayo and Phillips,[20] in presenting their series of cases of intussusception in children, reported the condition in an infant 3 weeks old. They found the operative mortality in cases of intussusception in which resection is done to be between 90 and 95 per cent. Hipsley,[21] in his review of the surgical pathology of intussusception, stated: "Intussusceptions generally occur in the thinner ileum, and, at any rate in children, practically never in the thicker-walled jejunum." The case presented in this paper illustrates this rare occurrence, intussusception in the jejunum of a newborn child.

REPORT OF A CASE

The mother, an 18 year old American of Polish descent, spontaneously delivered an apparently normal boy weighing 5 pounds and 14 ounces (2,665 Gm.). The pregnancy, the first, had been uneventful except for some nausea and vomiting during the first two months and, near term, slight edema of the hands and feet associated with frequency of micturition. The position was left occipitoanterior. Labor lasted eight hours, and delivery produced a first degree laceration.

On the first day of life one meconium stool was passed and vomiting of a green fluid was noted. On the second day the infant weighed 5 pounds and 3 ounces (2,353 Gm.). Breast feeding was instituted, but vomiting persisted, and another meconium-stained stool was passed. On the third day the infant weighed 4 pounds and 15 ounces (2,240 Gm.), a loss of 1 pound (454 Gm.) since birth. A hospital formula of equal parts of boiled water and milk with 5 per cent carbohydrate was given. Saline solution was given interstitially every eight hours to combat the dehydration. However, the loss of weight continued, and vomiting became projectile.

Physical examination at consultation [22] on the fourth day of life revealed a poorly developed boy weighing 4 pounds and 12 ounces (2,155 Gm.) and showing extreme dehydration, with sunken fontanels and loss of turgor of the skin. The infant was irritable, but no abnormal reflexes or evidence of tetany was found. Examination of the head, neck, chest and extremities revealed no abnormalities. Abdominal examination revealed a large cylindric inconstant mass extending from the upper left quadrant, at its costal border, diagonally downward and laterally across the abdomen to terminate below and to the right of the umbilicus. Massive peristaltic waves from left to right were readily obtained by lightly stroking the epigastrium or by feeding with a bottle. The liver was palpable but not enlarged.

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19. Steele, K. B.: Report of a Case of Intussusception in a Four Day Old Infant, Bull. Lying-In Hosp., New York **11**:56-58 (Jan.) 1917.

20. Mayo, C. W., and Phillips, J. R.: Acute Intussusception in Children, S. Clin. North America **13**:995-1003 (Aug.) 1933.

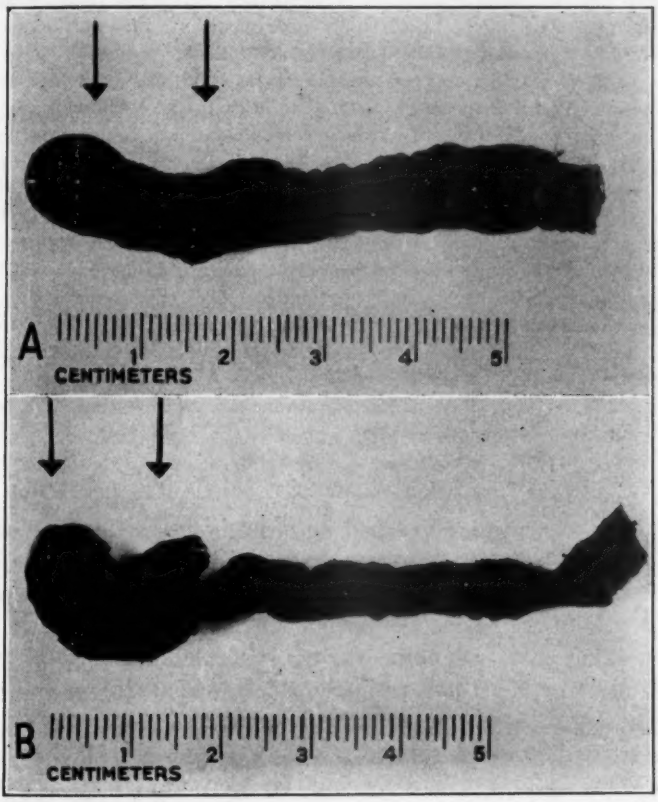
21. Hipsley, P. L.: Intussusception, Brit. M. J. **2**:717-721 (Oct. 19) 1935.

22. Dr. S. A. Kwasiborski referred the patient to me, Dr. Carl Kenning, roentgenologist, interpreted the roentgenograms, and Dr. W. H. Honor performed the operation.

The spleen was not palpable. Gastric lavage returned a bright yellow mucoid fluid. On rectal examination the exploring finger was stained with greenish viscid mucus.

Roentgen examination after the ingestion of barium sulfate showed that the material readily entered the enormously dilated stomach but that none left it within two hours. The diagnosis was obstruction at the pyloric-duodenal junction.

Saline solution was given intravenously and interstitially, in addition to direct transfusion of 50 cc. of blood. Atropine and phenobarbital were given, and suction



A, intussuscipiens incised to show the entire length of the intussusceptum. The arrows mark the advancing point of the intussusceptum and the section of jejunum entering the intussuscipiens. *B,* intussusceptum opened to show an enormous hemorrhage into the jejunal wall.

was initiated through a soft rubber catheter inserted through the nose into the stomach. Immediately before operation on the following day the transfusion was repeated. At this time the red blood cell count was 5,500,000 and the hemoglobin content 100 per cent (Dare); the bleeding time was three and one-half minutes. Before operation (fifth day) three black, tarry stools were passed, and for the first time in two days a moderate amount of urine, rich in urates, was voided.

After a right rectus approach into the abdomen the stomach and duodenum were found to be enormously dilated. Two intussusceptions were found; one was within 2 inches (5 cm.) of the ligament of Treitz and occupied 4 inches (10 cm.) of bowel; the second, which released itself, was 6 inches (15 cm.) distal to the first. The gangrenous intussusception was resected. The proximal portion of the jejunum was tied off, the distal portion was brought up, and an anterior anastomosis was made between it and the stomach.

The infant reacted fairly well, but four hours after operation he had a temperature of 103.6 F. and a pulse rate of 160 and became slightly cyanotic. Intravenous administration of dextrose was instituted, but slight vomiting persisted. Three brownish black, tarry liquid stools were passed. Although abdominal distention did not occur, death followed forty-two hours after operation.

The operative specimen was photographed before and after pathologic examination. The grayish white specimen, pictured in *A* of the accompanying illustration, showed on being opened (*B*) an irreducible brownish black intussusceptum within the resected part of the jejunum. The head of the intussusceptum measured 1.5 cm. in diameter and 3 cm. in length. The jejunum measured 0.7 cm. in diameter above the intussusception and 0.5 cm. below it. Further dissection and microscopic examination failed to reveal a physical cause for the intussusception.

Postmortem examination revealed marked wasting and desiccation, with bilateral bronchopneumonia and generalized peritonitis. The gastroenterostomy wound showed marked healing and was air tight and water tight, as was the blind end of the jejunum. The stomach and small intestine were collapsed and contained yellow partially digested milk. The descending colon contained a tarry pultaceous stool of digested blood. The abdominal wound on its cutaneous and peritoneal surfaces showed well advanced healing.

COMMENT

The first symptom, which had its onset immediately after delivery, was vomiting. The vomiting persisted and later became projectile. The vomitus contained bile but no macroscopic blood. The signs were extreme loss of weight and peristaltic waves in an enormously dilated stomach. The intussusception was not palpable, and only on the fifth day did digested blood appear in the stools. Constipation was present but not absolute. Roentgen examination disclosed no passage of barium sulfate from the dilated stomach.

Freilich and Coe,[23] in reviewing the literature, found 29 cases of jejunal intussusception from 1852 to 1934, to which they added 1. The youngest patient in this group was 4 months of age at operation, but the symptoms began at birth. In this case, reported by De Tarnowsky and Sarma,[24] the condition was attributed to a polyp of the jejunum. The child died in convulsions two hours after operation, which consisted of resection of a portion of the jejunum and repair by lateral anastomosis.

23. Freilich, E. B., and Coe, G. C.: Jejunal Intussusception, Ann. Surg. **105**: 183-191 (Feb.) 1937.

24. De Tarnowsky, G., and Sarma, J.: Polyp of Jejunum Causing Intussusception, S. Clin. North America **14**:879-881 (Aug.) 1934.

Of these 30 cases, in 7 the intussusception was diagnosed post mortem; in 2 it was triple jejunal in type; in 11 it was caused by polyps, in 2 by lipomas and in 1 each by lymphosarcoma, myoma, sarcoma, papillary adenoma, fibroadenoma, enlarged mesenteric nodes, fibroma, polypoid adenocarcinoma, leiomyoma, infiltrating papilloma and undifferentiated small tumor. In 4 others, including that which the authors reported, no cause was found. Twenty patients were operated on, with 6 deaths.

SUMMARY

A case of jejunal-jejunal intussusception is reported in which symptoms began at birth and gastro-enterostomy and resection of the irreducible intussusception were performed, with death forty-two hours after operation. This is the thirteenth case of intussusception during the newborn period and the first jejunal-jejunal occurrence reported in the literature.

Intestinal obstruction in the newborn presents a classic picture of (1) vomiting, the position of the obstruction determining whether the vomiting is projectile and whether the vomitus contains bile; (2) visible peristalsis; (3) abdominal distention and tympany, and (4) extremely rapid loss of weight (in this case, 1 pound in three days).

Intussusception may be also characterized by (1) a mass palpable on abdominal and/or rectal examination; (2) constipation; (3) the passage of blood-stained stools and/or blood on the finger on rectal examination; (4) colicky pain, evidenced by spasmodic flexing of the thighs on the abdomen and by crying, and (5) sweating, pallor and absence of normal resistance in the right lower quadrant on palpation (Dance's sign).

It is apparent that early diagnosis followed by prompt surgical measures offers the only hope of reducing the appalling mortality in cases of intestinal obstruction in the newborn. Preoperative preparation, which includes intravenous administration of saline solution to replace loss of fluid and chlorides, and transfusion, is of paramount importance. The longer the obstruction exists, the greater the probability of death after its release.

VARICELLA IN THE NEWBORN

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Varicella in the newborn is so unusual that it is looked on as a curiosity and its occurrence is worth reporting.

Newborn infants are protected against some infectious diseases by what may be regarded as natural immunity. Ehrlich [1] in his study of antitoxin immunity to ricin originally showed that passive transfer from immune mothers to their offspring occurs naturally. That antibodies are transferred through the placenta was shown by the work of Park and Zingher [2] on diphtheria, in which they compared Schick tests on mothers and on infants and demonstrated that the newborn infants almost invariably gave the same reaction as the mother. These observations were confirmed by Kuttner and Ratner,[3] who worked with the Schick test and made comparative titrations of the antitoxin content of the maternal and the cord blood. Park and Williams [4] concluded from these and from similar experiments that if a mother has a bacterial infectious disease and immunity develops she will transfer that immunity passively to her offspring. During late pregnancy, if the mother herself has an infectious disease and no miscarriage ensues, there is the possibility that active immunity will develop in the fetus in utero.

Similar experimental and clinical studies have been carried out with the infectious diseases caused by filtrable viruses. Aycock and Kramer,[5] on the basis of neutralization tests conducted with serums of mothers and their offspring, concluded that when the mother is immune to poliomyelitis there is passive transmission of immunity to the infant. The relative infrequency of poliomyelitis in infants under 1 year of age

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From the Willard Parker Hospital for Contagious Diseases, Department of Hospitals, New York.

1. Ehrlich, cited by McKinley, E. B., in Gay, F. P., and others: Agents of Disease and Host Resistance, Springfield, Ill., Charles C. Thomas, Publisher, 1935, p. 450.

2. Park, W. H., and Zingher, A.: Am. J. Pub. Health **6**:431 (May) 1916.

3. Kuttner, A. G., and Ratner, B.: Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

4. Park, W. H., and Williams, A. W.: Pathogenic Microörganisms, Philadelphia, Lea & Febiger, 1933, chap. 15, pp. 316-318.

5. Aycock, W. L., and Kramer, S. D.: J. Exper. Med. **52**:457 (Oct.) 1930.

is due in considerable measure to passive transmission of immune bodies to the young through the placenta. Brahdy and Lenarsky [6] reported several cases of poliomyelitis in the newborn in which the mother was essentially well during pregnancy but contracted the disease post partum, which indicates that newborn infants are susceptible when no passive immunity is inherited.

Measles in newborn infants has been reported by Kohn.[7] Eight cases were cited; several of the patients were exposed to measles post partum, the remainder being obviously infected in utero. It seems fair to assume that the 8 cases are convincing evidence that an infant born of a mother who has not had measles is definitely susceptible to the disease and displays no natural immunity. Congenital measles has also been reported by Reuss,[8] Canelli [9] and others.

Epstein [10] reported 5 cases of smallpox occurring on the eighth or ninth day after birth in infants of mothers who had the disease either during the last stage of pregnancy or shortly after delivery. Spalding [11] in a review of the subject cited 9 cases, described by various authors, of smallpox in mothers during the end of pregnancy. The infants, apparently healthy at birth, frequently manifested smallpox in the first few days of life, generally within seven to nine days. When the disease appeared earlier he attributed it to infection in utero; when later, to infection by contact.

As to vaccination, it is known that the newborn young of a vaccinated rabbit are immune to vaccinia, and this has been thought to be due to the passive transference of antibodies from the blood stream of the mother.

It is relatively simple to demonstrate immunity to diphtheria by the Schick test or to detect neutralizing substances in the blood of human beings or animals immune to such virus diseases as vaccinia, yellow fever, poliomyelitis and some forms of epidemic encephalitis.[11a] Since such laboratory tests are lacking for varicella, one can only assume by analogy that similar immunologic processes occur in this disease and that antibodies may be passively transferred from the mother to the fetus.

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6. Brahdy, M. B., and Lenarsky, M.: Acute Epidemic Poliomyelitis Complicating Pregnancy, J. A. M. A. **101**:195 (July 15) 1933.

7. Kohn, J. L.: J. Pediat. **3**:176 (July) 1933.

8. Reuss, A. R.: Die Krankheiten des Neugeborenen, Berlin, Julius Springer, 1914, p. 435.

9. Canelli, A. F.: Rev. franç. de pediat. **5**:668 (Dec.) 1929.

10. Epstein, A.: Arch. f. Kinderh. **60-61**:289, 1913.

11. Spalding, H., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 6, pp. 157-163.

11a. McKinley, E. B., in Gay, F. P., and others: Agents of Disease and Host Resistance, Springfield, Ill., Charles C. Thomas, Publisher, 1935, p. 1182.

Clinical observation and statistical studies give confirmatory evidence that these facts for the most part hold true for varicella. Since most women have had chickenpox, the occurrence of this disease in their young infants is therefore theoretically unlikely and actually rather unusual.

Mitchell and Fletcher [12] in a study of 775 cases of varicella at the Cincinnati General Hospital during the thirteen years from 1913 to 1926 presented the following data:

Age Incidence in 775 Cases of Varicella

Age.....	First 6 Mo.	6 Mo.-2 Yr.	2-6 Yr.	6-12 Yr.	12-20 Yr.	20 Yr. or Over
Percentage	1.4	11.7	36.4	24.2	6.8	19.4

The following tabulation, compiled by Gee [13] from records of the Children's Hospital of London, shows the age incidence among children with varicella in that institution:

Age Incidence in 727 Cases of Varicella

First 6 Mo.	6 Mo.-2 Yr.	2-6 Yr.	6-12 Yr.
80	234	332	81

At the Willard Parker Hospital in 1935, 1936 and 1937 and in 1938 to July there were 2,200 admissions of patients with varicella. The statistical age incidence is as follows:

Age Incidence in 2,200 Cases of Varicella

Age.....	Newborn	2 Wk.-6 Mo.	6 Mo.-2 Yr.	2-6 Yr.	6-12 Yr.	12-20 Yr.	20-30 Yr.	30-40 Yr.	40 Yr. or Over
Number.....	1	46	289	982	593	89	117	64	19
Percentage.....	0.05	2.15	13.15	44.6	26.95	4.04	5.3	2.9	0.86

The youngest patient was 2 days old and the oldest 65 years.

The fact that varicella confers immunity on its carrier and that this immunity may be transmitted from mother to child accounts for the rarity of this condition in the newborn. If, however, the mother never had chickenpox, the child may contract the disease soon after birth.[14]

The occurrence of varicella is rare even in the second two weeks of life. Sperk [15] reported the occurrence of 4 cases at the St. Anna's Hospital in Vienna during the period from 1905 to 1912. Mitchell and

12. Mitchell, A. G., and Fletcher, E. G.: Studies on Varicella: Age and Seasonal Incidence, Recurrences, Complications and Leukocyte Counts, J. A. M. A. **89**:279 (July 23) 1927.

13. Gee, cited by Schamberg, J. F., and Kolmer, J. A.: Acute Infectious Diseases, Philadelphia, Lea & Febiger, 1928, p. 302.

14. Lereboullet: Rev. gén. de clin. et de thérap. **51**:97 (Feb. 13) 1937.

15. Sperk, cited by Reuss.[8]

Fletcher [12] reported 1 case of varicella in the third week and 2 in the fourth week of life. At the Willard Parker Hospital statistics of the three and a half year period from January 1935 to July 1938 show but 1 such case, this in a 20 day old infant. Lereboullet and Moricand [16] reported a case of an infant who manifested varicella on the fourteenth day after birth. Apert [17] observed an epidemic of 12 cases of chickenpox in newborn infants 14, 16 and 17 days old or older.

The occurrence of varicella in the first two weeks of life is even rarer. A perusal of the literature reveals but 6 authentic cases. These are cases of so-called true congenital varicella, with the transmission of the virus through the placenta.

Pridham [18] (1913) was the first to report a case of congenital chickenpox. The patient was seen by that author four hours after delivery, at which time the infant presented the characteristic macular, vesicular, pustular eruption of the disease, which indicated that the eruption must have begun while the child was still in utero. The mother was apparently unaffected at the time, and it was not stated whether she had varicella previously.

In regard to this point there have been several misquotations from Pridham's paper. It is of particular significance, since this is the only case on record in which congenital varicella occurred in an infant whose mother did not have the disease at the time. The child, however, was born in a house where the disease had been present fourteen days before. The course was mild, the rash disappearing within a week.

It is recorded that Senator [19] saw a patient in whom the disease developed on the eleventh day of life, the infant presumably having been infected by the mother. Henderson [20] in 1934 described a case of chickenpox in an 8 day old infant. The mother had the disease at the time of parturition. General constitutional signs of illness in the infant were lacking. In March 1934 there appeared an account of another case of congenital varicella.[21] An 18 year old Chinese woman had the characteristic eruption of chickenpox for two weeks previous to delivery. Lesions of the macular and vesicular variety on the infant's face, chest, hands and legs were evident at birth. During the next few days there were successive crops of lesions, which disappeared in a week; no constitutional disturbances were observed. In a similar case, observed by

16. Lereboullet and Moricand: Arch. de méd. d. enf. **17**:228, 1914.

17. Apert, cited by Lereboullet.[14]

18. Pridham, F. C.: Brit. M. J. **1**:1054, 1913.

19. Senator, cited by Schamberg, J. F., in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1926, vol. 1, p. 529.

20. Henderson, W. B.: J. Pediat. **4**:668 (May) 1934.

21. Cosgrove, A. K., and Samuel, J.: Malayan M. J. **9**:68 (March) 1934.

Mitchell and Fletcher,[21a] a child with a varicella eruption was born of a mother who was also suffering from the disease.

Baron [22] reported a case of chickenpox in an 8 day old infant; the mother had the disease when the baby was born. The child was breast fed with the customary precautions, without being isolated. On the fourth day of illness, the infant became cyanotic, had convulsions and died.

In a review of the French literature, Baron could find but few similar reports. He concluded that if a woman contracts chickenpox in the terminal stage of pregnancy or during labor, she is not able to transmit immune bodies for chickenpox to her infant, who remains susceptible to the disease and should be isolated.

Ivenskaya [23] in 1929 and Troetskiy [24] in 1932 reported studies of varicella in full term and premature infants. They independently concluded that premature and ill infants are less likely to have chickenpox than normal infants. They mentioned the occurrence of varicella in an infant a few days old, but no details were given.

An additional case of varicella in a newborn child, observed and studied at the Willard Parker Hospital, is presented.

REPORT OF A CASE

A 24 year old married woman entered the Willard Parker Hospital on March 28, 1938, accompanied by a 2 hour old, full term, normal baby girl. Eight days previously the mother had presented a maculopapular eruption which later became vesicular. She remained at home unattended until the process of labor caused her to go to a hospital in New York, where the child was spontaneously delivered within an hour. The cutaneous eruption was diagnosed as varicella, and the patient was transferred to the Willard Parker Hospital.

On admission the mother appeared to be moderately ill, with a temperature of 100 F. The usual early postpartum findings were present. The skin showed a generalized eruption consisting of a few vesicles, many crusted lesions and a small number of pigmented crater-like lesions. The diagnosis of healing varicella was confirmed. The physical examination otherwise gave negative results.

The infant weighed 5½ pounds (2,495 Gm.) and was well nourished and well developed. No congenital abnormalities were found. The skin was of good color and tone and free from any lesions. The infant and mother were kept together in a large room isolated from all other patients. The infant was fed by formula for the first twelve hours and then put to breast on a four hour schedule with a supplementary formula until the third day, when it was fed entirely by breast. A thorough examination on the day after admission revealed that the infant was perfectly normal, with a clear skin. Forty-eight hours after birth a small single

21a. Mitchell, G. A.: Personal communication to the author, Aug. 12, 1938.

22. Baron, F.: Nourrisson **23**:157 (May) 1935.

23. Ivenskaya, E. A.: J. izuch. rann. detsk. vozr. **9**:504, 1929.

24. Troetskiy, A. Y.: J. rann. detsk. vozr. **12**:391, 1932.

papule was observed on the right index finger. The next day another isolated lesion was noted on the left thigh, and the original lesion had become a vesicle. On the fourth day there appeared twelve to fifteen lesions, which were for the most part vesicles. These were located on the face, neck, chest and extremities, as shown in the accompanying illustration.

The infant then was making good progress and taking the breast well and had regained her birth weight. On the fifth day the early lesions were beginning to crust. A crop of fresh vesicles had made their appearance. At no time was there elevation in temperature or systemic involvement. The lesions for the most part became crusted, and practically all disappeared within ten days. Except for a single lesion on the left buttock which became infected and required incision, the disease ran its usual benign course. The infant was discharged from the hospital

The patient on the fourth day of life.

with the mother on the fifteenth day, in good condition, weighing 6½ pounds (2,948 Gm.). The skin was clear except for a few small pigmented scars of varicella lesions and a well healed incision on the left buttock.

COMMENT

The occurrence of varicella in newborn infants is a rarity. A thorough survey of the literature reveals but 6 cases, to which I have added a seventh.

In 5 of the 6 cases of congenital varicella previously reported the disease apparently ran a benign course. This was also true in the case which I observed. In only 1 instance, the case reported by Baron, was there a fatality, and it is not clear whether varicella was a contributory cause of death.

The incubation period of varicella contracted by exposure is held to be eight to twenty-one days, usually about fourteen days, and

therefore there is good reason to believe that varicella in neonatal life represents transmission of the etiologic agent, the filtrable virus, through the placenta in utero.

It is obvious that the development of immunity by the mother in the case here reported was not sufficiently rapid to prevent infection of the full term fetus.

Congenital varicella should be considered in the differential diagnosis of any vesicular-pustular eruption in a newborn child, as impetigo has been confused with neonatal varicella on several occasions.

Although experimental proof is lacking, it seems from clinical evidence that infants of mothers who never had varicella or of mothers in whom it developed during the last month of pregnancy are susceptible to the disease.

SUMMARY

A review of the literature of varicella in the newborn is given. A case is presented in which the rash appeared on the second day of life of an infant whose mother was suffering from the disease at the time. I believe that this represents transmission of the disease in utero.

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AGENESIS OF THE LUNG

REVIEW OF THE LITERATURE AND REPORT OF A CASE

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A careful review of the literature indicates that the total failure of a lung to develop is exceedingly rare. Only 37 authentic cases have been reported. Twenty-four of the patients were children under 12 years of age. We wish to add to this series a case of our own.

The patients in the recorded cases had the following age distribution: 3 stillborn infants (Gruber [1] and Minne and Gernez [2]); 5 infants under 1 week of age (Maschka,[3] Théremin,[4] Miller,[5] Hanson [6] and Findlayson [7]); 13 infants under 6 months of age (Hein,[8] Stein,[9] Théremin,[4] Miller,[5] [2 cases], Gross,[10] Gilkey,[11] Finner,[12] Hepner,[13] Knott,[14] Dyson,[15] Toni [16] and Hurwitz and Stephens [17]), 2 infants under 3 years

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* Fellow of the Otho S. A. Sprague Memorial Institute, Chicago, 1937-1938.

1. Gruber, W.: Oesterr. Ztschr. f. prakt. Heilk. **16**:7, 1870; Virchows Arch. f. path. Anat. **102**:11, 1885.
2. Minne, J., and Gernez, L.: Ann. d'anat. path. **10**:503, 1933.
3. Maschka: Allg. Wien. med. Ztg. **7**:78, 1862.
4. Théremin, E.: Rev. mens. d. mal. de l'enf. **2**:554, 1884.
5. Miller, N. F.: Trudi Obsh. dietsk. vrach. **3**:32, 1894-1895.
6. Hanson, R.: Babe with One Lung, J. A. M. A. **37**:701 (Sept. 14) 1901.
7. Findlayson: Proc. Anat. Soc. Gr. Britain & Ireland, 1901-1902, p. 38.
8. Hein: Wchnschr. f. d. ges. Heilk., 1837, p. 536.
9. Stein, cited by Fürst, L.: Missbildungen der Lunge, in Gerhardt, C.: Handbuch der Kinderkrankheiten, Tübingen, H. Laupp, 1878, vol. 3, pt. 2, p. 553.
10. Gross, W.: Beitr. z. path. Anat. u. z. allg. Path. **37**:487, 1905.
11. Gilkey, H. M.: J. Missouri M. A. **25**:296, 1928.
12. Finner: Clifton M. Bull. **18**:35, 1932; cited by Hurwitz, S., and Stephens, H. B.: Am. J. M. Sc. **193**:81, 1937.
13. Hepner, F.: Arch. f. Kinderh. **103**:92, 1934.
14. Knott, A.: Ztschr. f. Kinderh. **56**:338, 1934.
15. Dyson, J. E.: J. Iowa M. Soc. **24**:442, 1934.
16. Toni, C.: Clin. pediat. **16**:241, 1934.
17. Hurwitz, S., and Stephens, H. B.: Am. J. M. Sc. **193**:81, 1937.

of age (Yampolsky, Fowler and Stephens[18] and Mitchell[19]); 1 child 8 years of age (Ellis[20]) and 1 child 12 years of age (Tebbutt[21]). Adults have been reported on by Haberlein[22] (2 cases), Herrero,[23] Bell and Bell[24] (2 cases), Jarisch,[25] Levy,[26] Muhamed,[27] Dannheiser,[28] Heerup,[29] Welsch[30] and Tichomiroff.[31] The ages of this group varied between 19 and 72 years. Agenesis of the left lung occurred in 24 of the 37 cases. In the 33 cases in which sex was recorded, 20 patients were males and 13 females. Mitchell's case is extremely interesting.

REPORT OF CASE

A. M., a girl aged 72 hours, was admitted to the Children's Memorial Hospital on Feb. 25, 1938, because of cyanosis since birth. The child was born at full term with vertex delivery without the assistance of instruments. The delivery was easy and of short duration. The birth weight was 5 pounds and 4 ounces (2,381 Gm.). The records of the maternity hospital listed no abnormalities at birth, except that the child had a weak cry and was resuscitated with difficulty. On the day of birth she had a choking cyanotic episode, which required that she be kept continuously in an oxygen tent. A second bout of cyanosis occurred on the second day of life, despite oxygen therapy, but no further attacks occurred until her admission into the Children's Memorial Hospital. The child nursed well but had not cried since birth. The family history was essentially irrelevant except that the mother had had hyperemesis gravidarum up to the sixth month.

Physical examination revealed a small, well formed and well nourished newborn girl of good color. There was no icterus, rash or other abnormality except in the chest. The thorax was poorly formed. It was narrow in both the anteroposterior and the lateral diameter. The breathing was exaggerated on the left side. There was lagging of the respiratory movements on the right. Percussion elicited markedly dull to flat sounds from the entire right side of the chest, both in front and behind, and there was marked suppression of breath sounds. Neither bronchial breathing nor bronchophony was heard. The heart was definitely situated in the right side of the chest. The clinical impression was massive fetal atelectasis of the right lung.

On the patient's admission the hemoglobin content was 95 per cent (Sahli), 5,000,000 red cells per cubic millimeter. There were 10,300 leukocytes, of which

18. Yampolsky, J.; Fowler, C. D., and Stephens, E.: Arch. Pediat. **55**:293, 1938.
19. Mitchell, H. E.: Ohio State M. J. **32**:950, 1936.
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22. Haberlein, cited by Hurwitz and Stephens.[17]
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26. Levy, C. S.: Am. J. M. Sc. **159**:237, 1920.
27. Muhamed, K. S. N.: Indian M. Gaz. **58**:262, 1923.
28. Dannheiser, F.: Beitr. z. path. Anat. u. z. allg. Path. **76**:87, 1926.
29. Heerup, L.: Hospital **70**:1165, 1927.
30. Welsch, K.: Frankfurt. Ztschr. f. Path. **36**:192, 1928.
31. Tichomiroff, M.: Internat. Monatschr. f. Anat. u. Physiol. **12**:24, 1895.

17 per cent were polymorphonuclears and 83 per cent lymphocytes. Four nucleated red cells per hundred white cells were counted. The urine was normal, and the Wassermann reaction was negative.

Repeated roentgen studies revealed hyperaeration of the left lung with complete obliteration of the right pleural cavity, the entire heart being displaced to the right of the spine. On the left, the intercostal spaces were narrowed and there was a synostosis between the first, second and third ribs posteriorly (fig. 1). These findings were interpreted as indicating high grade collapse of the entire right lung with hyperaeration of the left lung.

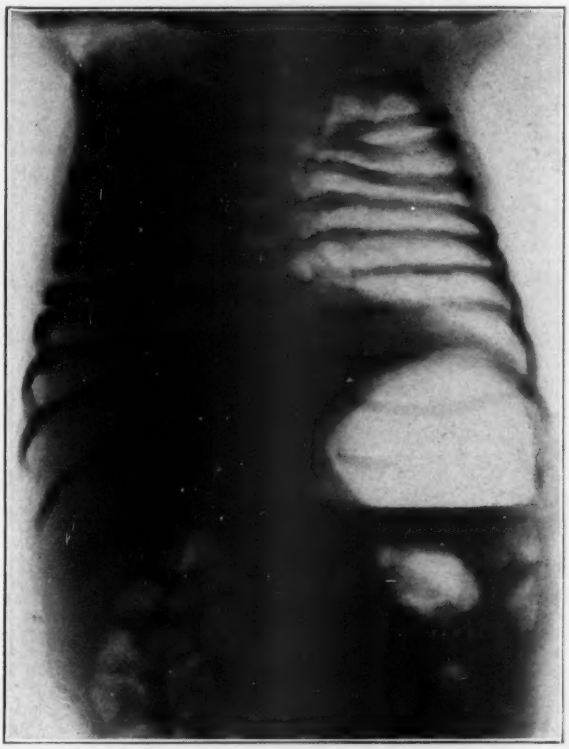

Fig. 1.—Roentgenogram of the chest, showing complete obliteration of the right pleural cavity and premature synostosis of the left first, second and third ribs.

On February 27 the child was seen by Drs. Brennemann and Holinger, who were of the opinion that she should be examined with the bronchoscope, in order that it might be determined whether there was any obstruction or pathologic condition that could be removed or remedied. On March 4, after attempted bronchoscopic study, Dr. Holinger wrote the following note:

"The larynx was exposed, and the bronchoscope was passed with difficulty. The trachea deviated so far to the right that the bronchoscope could not be advanced. It was withdrawn, and a small bronchoscopic aspirator was passed through the larynx. The aspirator could not be advanced to the bifurcation of the trachea. Since the carina was not reached, the main bronchi were not visualized."

On the following day (March 5) the child had a severe cyanotic attack and died, at the age of 10 days. She was afebrile throughout her stay in the hospital.

Postmortem Examination.—Gross Observations: A complete autopsy was permitted, and multiple congenital anomalies were observed.

There was synostosis of the first, second and third left ribs posteriorly (fig. 1).

When the sternal plate was removed, the heart and pericardium were seen to be situated almost completely in the right side of the thorax, no right pleura or pleural cavity being demonstrable. The heart measured 5 cm. across its widest portion, and its right side was moderately dilated. A right lung could not be found. The thymus was of normal size and weighed 15 Gm. The pulmonary artery, the aorta and the great vessels were normal anteriorly. The pulmonary artery measured 1.5 cm. in diameter and the aorta 1 cm.

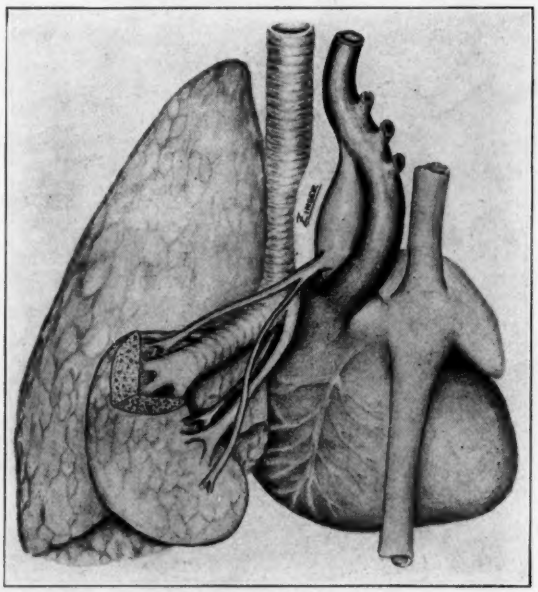

Fig. 2.—Posterior view of the heart, great vessels and left lung (artist's drawing). Note constriction of the trachea just above the carina, the single pulmonary artery to the left lung, the ductus arteriosus and fetal atelectasis of the lower lobe of the left lung.

Filling the entire left pleural cavity there was a single emphysematous hypertrophied lobe. Its inferior border was in direct relation with the left leaf of the diaphragm. The lobe was dull; the color varied from red to gray, and the rib markings were prominent. Attached to the inferior surface of this single air-containing lobe there was a small rounded firm purple-red nodule of tissue which measured 3 by 1.5 by 2 cm. It did not contain air; it was covered by the same fascia and fibrous tissue as the emphysematous lobe. It was considered that the emphysematous lobe was anatomically the upper lobe of the left lung and the nodule which contained no air the rudimentary lower lobe of the left lung. This was confirmed when the thoracic content was removed and examined from behind (figs. 2 and 3). The trachea, as it passed downward, divided into a single large

left upper bronchus and a small lower bronchus and continued directly to the upper and the lower pulmonary lobes. The trachea curved to the right and then to the left in its downward course. Just above the upper left bronchus it narrowed, the diameter measuring 3 mm., in contrast to a subglottic tracheal diameter of 5 mm. The large left upper bronchus was normal. The left lower main bronchus ended in blind pouches after dividing twice in the rudimentary lower pulmonary lobe.

On posterior examination a right lung could not be found, and no bronchus or vestiges of bronchi coming from the right side of the trachea were discovered.

Fig. 3.—Photograph showing the heart and left lung from behind and the genitourinary tract. There is congenital absence of the left kidney and ureter. The single fallopian tube is cut open.

Only the two previously described branches were present. Attached to the normal pericardium on the right was a small mass of gray-yellow lobulated fatty tissue which measured 2.5 by 2 by 0.5 cm.

The musculature and valves of the heart were normal. The myocardium of the right ventricle measured 8 mm. in thickness and that of the left 9 mm. The right auricle, however, was three times as large as the left. Posterior examination revealed no abnormalities of the superior and inferior venae cavae. However, when dissection of the heart and blood vessels was complete it was noted that the aorta and the pulmonary artery joined at a distance of 2 cm. from the cardiac

base through a patent ductus arteriosus. Just before the pulmonary artery joined the aorta through this ductus there was high grade stenosis of its lumen, which barely permitted the passage of a small probe.

At a distance of 0.5 cm. from the pulmonary valve there arose a single pulmonary artery, which measured 4 mm. in diameter. It passed backward and entered the hilus of the upper pulmonary lobe on the left side. Before doing so it gave off a fine, slender patent branch 1 mm. in diameter, which went to the

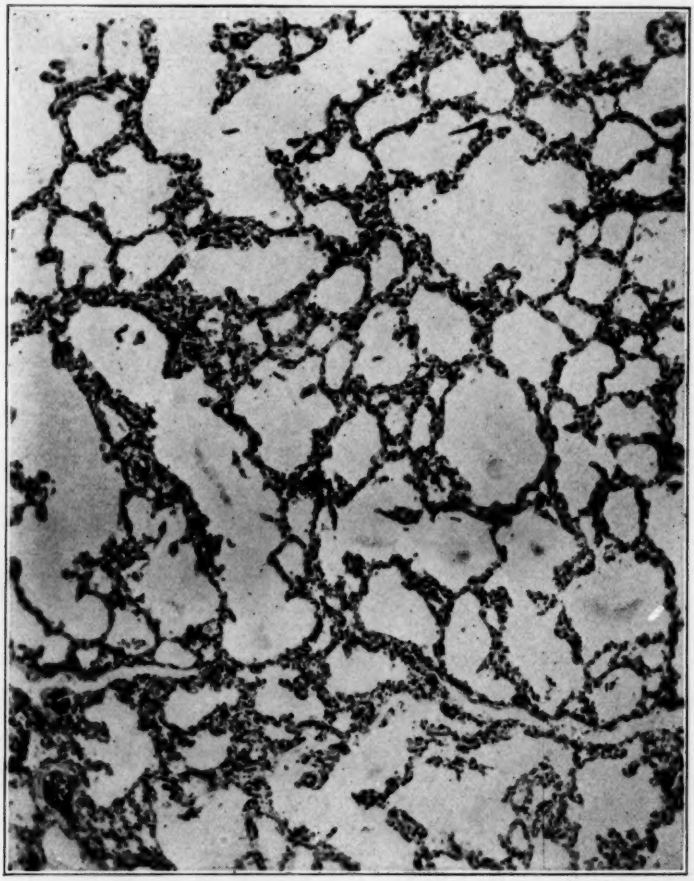

Fig. 4.—Emphysema of the upper lobe of the left lung. Hematoxylin and eosin stain; × 70.

atelectatic lower lobe. This was the only blood supply of the lobe. The pulmonary vein to the left auricle was single. It consisted of one large vein from the upper lobe, which was joined by several smaller veins from the lower lobe. In addition to the anomalies just described, there was a partially patent foramen ovale, which measured 0.5 cm. at its widest diameter.

There was complete absence of the left kidney and ureter. The right kidney, adrenal and ureter and the left adrenal were normal. There was no left renal

artery or vein. The blood supply to the left adrenal arose from the abdominal aorta, and its venous return emptied into the inferior vena cava. The right ureter was partially stenosed at a point 1.5 cm. above the urinary bladder. The latter was normal except that it had but one ureteral orifice, that of the right ureter. The uterus and vagina were normal. Only one ovary and fallopian tube were present, and these were attached medially to the top of the fundus of the uterus (fig. 3).

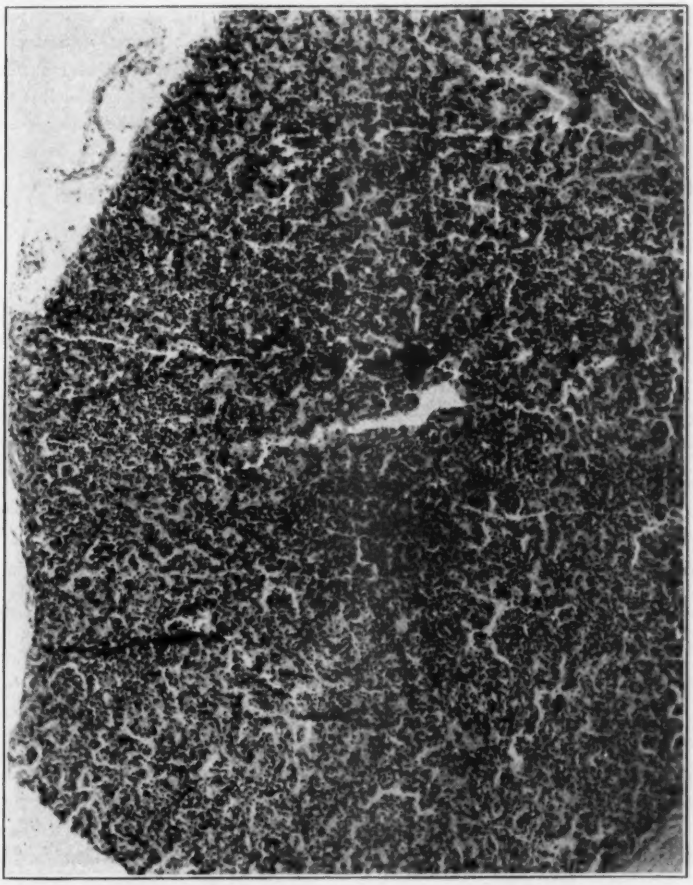

Fig. 5.—Fetal type of atelectasis of the lower lobe of the left lung. Hematoxylin and eosin stain; × 70.

No other abnormalities were noted.

Postmortem Blood Culture: This yielded Bacillus alkaligenes.

Microscopic Observations: The sections were prepared with pyroxylin and with hematoxylin and eosin stain (figs. 4 and 5). In most of the sections from the upper left pulmonary lobe there was moderate emphysema, with a few focal areas of atelectasis. The alveolar walls were moderately thickened and hyperemic. There was no edema or exudate. The blood vessels and small bronchi were normal.

In all sections from the lower left pulmonary lobe there was fetal atelectasis, characterized by whorls of tissue composed of thick cuboidal epithelium. No definite alveoli or air-containing tissue was found. In a few irregular areas red blood cells and a few polymorphonuclear cells were present. The blood vessels were normal, but the small bronchi were collapsed and nonpatent. No cartilage or muscle was found in cross sections.

Anatomic Diagnosis: This was congenital absence of the right lung, right bronchus and right pleura; fetal atelectasis of the lower lobe of the left lung; hypoplasia of the lower lobe of the left lung; patent ductus arteriosus; single pulmonary artery (left); stenosis of the pulmonary artery; patent foramen ovale; dilatation and displacement of the heart to the right; hyperemia of the viscera; emphysema of the upper lobe of the left lung; congenital absence of the left kidney and ureter; single ovary and fallopian tube; stenosis of the right ureter; posterior synostosis of the first, second and third left ribs.

The cause of agenesis of a lung is obscure. Meckel and Fleischmann [32] explained the condition on a phylogenetic basis, comparing it with that in reptiles. Klebs [33] stated the belief that agenesis of the right lung is due to the excessive tension of the amnion when the embryo is rotated to the left, development of the right lung being prevented. This fails to explain absence of the left lung. Eppinger [34] suggested that enlargement and displacement of the thymus was responsible for failure of development of the left lung in Tichomiroff's case. Tichomiroff believed that hydrops foetalis or some other early intrathoracic fault or infection was the cause of this defect. However, all of these theories are inadequate and inconclusive. The most plausible and rational explanation is that of Schwalbe.[35] He ascribed agenesis of the lung to a developmental error of endogenous origin — faulty germ plasm, as it were — primary in the pulmonary vascular and respiratory systems.

Schwalbe's explanation fits in with the supposed embryonic development of the respiratory system as described by Arey: [36]

A groove-like evagination arises on the ventral side of the esophagus in the 3 mm. human embryo. From the enlarged posterior ends of the groove, two small lung buds grew out. Later in the development the predestined anlage of the trachea and esophagus becomes separated by a constriction interrupted at the cephalic end by the larynx which can be seen in the embryo at the end of the fifth week. Muscle fibers and cartilaginous rings differentiate from the surrounding mesenchyme by the end of the seventh week. In a later development of the lung buds hollow evaginations grow out into the envelope of connective tissue, enlarge rapidly, and branch to produce the tree-like tubular system. On the fine terminal tubules arise small out-growths which constitute the alveoli.

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32. Meckel and Fleischmann, cited by Dannheiser.[28]

33. Klebs, cited by Knott.[14]

34. Eppinger, cited by Knott.[14]

35. Schwalbe, E.: Die Morphologie der Missbildungen des Menschen und der Tiere, Jena, Gustav Fischer, 1909-1913, vol. 3, pt. 2, chap. 8, p. 763.

36. Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1937, p. 210.

There may be complete absence of either lung; in some cases there remains a rudiment of lung tissue, which may be at the end of a bronchus, on the side of the trachea, attached to the esophagus or in the mediastinum. The pleura on the affected side may be completely or partially absent but is usually the latter. The cavity may be filled with fluid, but ordinarily it contains the displaced heart and mediastinal structures, fatty tissue or persistent thymus. The bronchus on the affected side, if present, is small in diameter and short, usually ending in a blind pouch. When there is no vestige of a bronchus, the trachea may enter the normal lung without dividing or may divide into two or three primary bronchi before entering the lung. Narrowing of the tracheal lumen and an increase in the number of its cartilaginous rings are common. The pulmonary blood vessels of the affected side are usually absent, and a single pulmonary artery supplies the hypertrophied lung. The aortic vessels may arise from a common trunk. The venous return of the unaffected side reaches the left auricle by one or more vessels or empties directly into the vena azygos.

The remaining lung is almost always hypertrophied and emphysematous, with abnormal lobulations. Pneumonia is a common complication. Bronchiectasis has been noted. Many associated congenital anomalies have been described, such as anal stricture, absence of the diaphragm, esophagotracheal fistula, accessory thymus, hypertrophic thymus, hypoplasia of the face, hernia of the diaphragm on the affected side, dextrocardia, exencephaly, absence of the vagus nerve, various bony anomalies, such as absence of the radius, anomalous kidney vessels, pericardial adhesions, dermoid of the eye and cardiac anomalies too numerous to mention.

Absence of a lung does not preclude longevity. In the recorded cases 11 patients lived beyond their nineteenth year. The 3 oldest patients were 58, 65 and 72 years of age, respectively, and all died of causes unrelated to the agenesis of the lung.

The symptomatology of congenital absence of a lung is variable. Rarely are the symptoms distressing, although dyspnea, cyanosis, stertorous breathing and failure to thrive are common in the younger patients. The thorax is usually symmetric, but it may be flattened on the affected side. Scoliosis toward or away from the affected side may occur. Movement on the affected side is always diminished to some degree. The heart and the mediastinal structures are always displaced to the side on which the lung is absent, and the apical impulse of the heart is pronounced. Dulness or flatness of the affected side is usual, but occasionally there is resonance because of hypertrophy and emphysema of the remaining lung. Breath sounds may then be altered; most frequently they are absent, suppressed or bronchial. Roentgen examination reveals a dense homogeneous shadow on the affected side, with

shifting of the heart and mediastinal structures to that side. The diaphragm of the affected side may be elevated and the intercostal spaces narrowed. The usual interpretation of the roentgenograms is massive or fetal atelectasis.

The differential diagnosis in cases of congenital absence of a lung is extremely difficult. In only 2 cases has diagnosis been made before death (Gilkey [11] and Welsch [30]). Atelectasis, fetal or massive, is the most frequent diagnosis. Pneumonia, hydrothorax, paralysis of the diaphragm, diaphragmatic hernia and foreign body in a bronchus must be considered. It may be possible to establish a clinical diagnosis by bronchoscopic study, although the usual age of the patient and the size of the trachea and of the main bronchi are limiting factors. However, the diagnosis of congenital absence of a lung has been made by combining the clinical history and the physical and roentgen observations.

SUMMARY

A case of congenital absence of the right lung in a girl 10 days old is presented. Necropsy revealed other congenital anomalies. Bronchoscopic examination was not helpful as a diagnostic procedure, owing to the small size and marked deviation of the trachea. A detailed review of the literature is given. No etiologic explanation is offered.

Dr. Joseph Brennemann and Dr. L. B. Arey gave assistance and suggestions, and Mr. Charles Zinser made the anatomic drawing.

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Progress in Pediatrics

IMPORTANCE OF THE SENSITIZATION MECHANISM IN THE CLINICAL PHENOMENON OF ALLERGY

POSSIBLE CAUSE AND PREVENTION

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AND
H. E. THELANDER, M.D.
SAN FRANCISCO

The theory of human allergy is based on analogy to anaphylaxis in guinea pigs, in which sensitization to a specific protein is succeeded by shock when the allergen is later reinjected. Serum disease is an inadvertent experiment which sometimes closely simulates experimental anaphylaxis, but in most clinical allergies the parallel is less complete. Most investigators of human allergy have been content to leave unexplained the mechanism of sensitization and have devoted themselves to the problem of averting the shock component. The clinician must admit that methods of prevention and treatment of allergic reactions in the hypersensitive patient are unsatisfactory. When a state of hypersensitiveness is present, shock (secondary) phenomena may readily be induced by inhalation, ingestion, injection or mere application of the specific allergen to the skin. Detection and elimination of specific allergens and the use of graduated dosage for the development of tolerance or antianaphylaxis (seldom convincingly attained) frequently fail, and transient success is often succeeded by a series of sensitizations to other allergens, which, in turn, have to be treated.

The fundamental problem of human allergy concerns not the phenomenon of shock but the mechanism of production of hypersensitiveness; once sensitization has occurred it probably constitutes an irreversible state, for which control measures are, not surprisingly, more or less unsuccessful. The approach to the problem which may point the way toward practical control is the study of the process of sensitization and of methods for its prevention.

It has, of course, been proposed that the allergic patient has a peculiarity of constitution which renders him especially susceptible to

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sensitization and to shock. This may well be a factor, but clinical experience indicates that it cannot be the most important. Unmistakable allergic symptoms are so common as to suggest that few children can be completely insusceptible to their occurrence. The more closely children are observed, the more frequently will these symptoms be detected; furthermore, there is little doubt that they are increasing, although improved resourcefulness in management may make for fewer severe manifestations. It is common experience to find infants who, at least for a time, cannot tolerate fish oils, orange juice or wheat or who better tolerate milk which has been modified in its allergenic constituents. The popularity of foods of lessened allergenic properties, such as dried or evaporated milk or substitutes for cod liver oil, attests the commonness of the problem. Not only do alleregic signs frequently appear spontaneously, but they are almost invariably produced when appropriate amounts of serum are parenterally introduced. All this suggests that an exogenous rather than a constitutional factor is of fundamental importance.

The presence of unaltered protein in the blood stream is hardly the critical factor, for this must be accepted as fairly common and normal. When local sensitization is secured, as by the Prausnitz-Küstner phenomenon, ingestion of the specific allergen produces reaction in the sensitized area, which indicates the probable presence of the allergen in the circulation. The transfusion of blood withdrawn from a donor after a meal will sometimes produce severe reaction in an allergic recipient. Unaltered food proteins have been demonstrated in breast milk, which they must have reached by way of the maternal circulation. The entrance of foreign proteins into the circulation must be regarded as probably physiologic; some additional factor must cause sensitization to occur.

Modern conditions have led to a decrease in breast feeding, but the fact that many infants receive cow's milk instead of, or in addition to, breast milk is probably not the sole factor responsible for sensitization. The breast-fed infant receives some foreign protein in the breast milk and not infrequently becomes sensitive to it; allergic symptoms are commonly found in the baby fed entirely by breast.

Sensitization can hardly be attributed to a gross defect in nutrition. The allergic state is common, and probably increasing, at a time when the nutrition, health and entire status of infants have been generally improved. The most common excitants of allergy are the food proteins commonly and properly given, not those of less common use or of dubious propriety. Infants fed essentially identical diets may escape sensitization or may become sensitive to different proteins.

Allergic conditions of infants occur at a time of life when simplicity of regimen, diet and environment and the usual absence of illness make

for a problem which is attended by fewer variables than is the more complex problem of the older child or the adult. The human infant may be observed under conditions so carefully standardized as to make him an ideal subject for study of a process which becomes almost inextricably complex in later years and cannot adequately be studied in experimental animals. It is scarcely overoptimistic to propose that from the study of allergy in infants some fairly simple and obvious factor may be gleaned to explain the production of sensitization and perhaps to shed light on conditions encountered in later years.

A number of facts indicate the plausibility of the hypothesis that a lack of an adequate amount of vitamin C may be essential to the production of hypersensitiveness as it occurs in infancy. Some of these may quickly be mentioned:

1. Bezredka demonstrated that in the guinea pig sensitization by ingestion was best accomplished by using animals fed a scurvy-producing diet.

2. Animals who synthesize their own vitamin C, such as rats and dogs, are refractory to sensitization.

3. There are innumerable evidences that vitamin C is intimately connected with the immunity mechanism of the body and that allergy is definitely related to the function of immunity, although the precise relationship is difficult to define.

4. Vitamin C is intimately related to the permeability of the tissues, as illustrated by the association of hemorrhage and similar manifestations with deficiency of this vitamin. It seems plausible that its lack may conduce to a more intimate exposure of the cells to foreign protein in the circulation. Allergic patients have repeatedly, but not constantly, been shown to lack vitamin C in the blood and to be somewhat improved by its ingestion. Do they lack it especially when susceptible to sensitization?

5. Before birth the infant receives vitamin C only by way of the maternal blood. Difficulties of nutrition during gestation must frequently lead to periods of reduction in the supply of vitamin C; infants are unquestionably sometimes sensitized in utero. The infant fed exclusively by breast receives an adequate ration of vitamin C only if the maternal supply is adequate to secure proper concentration in the breast milk. Sensitization occurs in the infant who is fed only by breast. Boiled cow's milk, evaporated milk and dried milk contain inadequate amounts of vitamin C, as do most other foods which comprise the common diet of the modern infant. Orange juice or other sources of the vitamin are recognized as essential to the artificially fed baby, but administration is commonly not begun for a variable time after birth,

and frequently amounts which are inadequate constitute the sole supply for many weeks. Although continued deficiency results in scurvy, this usually appears at about the sixth month and only after a considerable period in which failure to gain is indicative of prolonged deficiency of vitamin C. Lack of vitamin C for only a short time may favor the development of sensitization; in a majority of cases the deficiency may be overcome so quickly as to prevent recognizable scurvy, and yet the sensitization may remain.

During the period of life when intake of vitamin C is most poorly insured, from birth to the age of 4 months, the baby receives almost exclusively the foods which most commonly provoke the allergies of infancy and childhood: milk, fish oil, egg, wheat and orange juice. Orange juice, which is usually relied on to supply an adequate vitamin C ration, is not the physiologic source in infancy, and the fact that it contains vitamin C need not prevent sensitization to orange protein, which frequently occurs. Allergy is common among Chinese in San Francisco, who consume little fruit juice and give it sparingly to infants. It has frequently been observed elsewhere, especially in Scandinavia, where because of the paucity of citrus fruits it is difficult to keep an adequate amount of vitamin C in the diet. Until the advent of synthetic vitamin C many infants known to be allergic were permitted to continue for long periods with an extremely meager intake. It has been a common experience that allergic symptoms in these infants have been controlled by removal of offending proteins from the diet, only with development of sensitization to the substituted proteins. Even later in life sensitization to food protein is seen to occur after enteritis, other infections and various nutritional states in which intake of vitamin C is restricted. Spontaneous allergy is almost entirely confined to human beings, who, alone in the animal kingdom, subsist largely on cooked foods in which thermolabile vitamin C has been destroyed.

The essentials of this hypothesis may be summarized as follows: The capacity for allergic sensitization and subsequent shock phenomena is fairly universal; under ordinary conditions it is spontaneously exhibited by many persons, and under properly designed conditions (of parenteral administration) it is revealed by nearly all. The essential variation of the allergic from the normal person is that he has acquired, or has the capacity to acquire, hypersensitiveness by the ingestion of protein or by absorption apart from artificial injection. Entrance of foreign protein into the circulation occurs fairly normally and cannot be the sole determining factor for the production of hypersensitiveness.

The function of vitamin C in protection against sensitization is suggested by many facts. These include the bearing of this vitamin on the sensitization of experimental animals by ingestion, its relation to

immunity and to tissue permeability, the common occurrence of successive sensitizations of allergic patients, who frequently lack vitamin C, the occasional inadequacy of the vitamin in maternal blood and in breast milk, its lack in the artificial diet, unless added in fruit juices or other sources, and its deficiency in many disease states which favor the production of allergy.

This is not to say that the allergic infant must constantly be deficient in vitamin C. Once sensitization has occurred, shock may readily be produced by a different set of factors, and the continued presence of sensitization may be due to irreversible phenomena, which are not altered by correction of the factors which first produced it. Other factors affect the allergic state, and different factors may have a different bearing under varying conditions.

It has recently been stated by Bromfenbrenner that inadequacy of vitamin C predisposes to the development of shock when sensitized guinea pigs are given the specific allergen by ingestion. This seems entirely consistent with our hypothesis but does not alter our opinion that the mechanism of sensitization (and not of shock) is the most fecund for investigation of the fundamentals of the problem of allergy. It is our further belief that the human infant presents the essentials of the experimental study of this problem.

For some time we have routinely been giving ample daily amounts of ascorbic acid (usually 25 mg.) after the first few days of life. It is our opinion that colic (which is the only common allergic response of early infancy) is consistently thereby reduced. We propose to study our subjects for the development of later allergies and to try to determine as accurately as possible the probability that early deficiency of vitamin C causes the later allergies which are seen in pediatric practice.

CAUSES OF PREMATURITY

I. REVIEW OF THE LITERATURE

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Many factors have been reported to have an influence in causing prematurity. We have reviewed the results of these previous studies and classified them in an attempt to find the most common predisposing factors. This review is preliminary to our own clinical and statistical investigation of the subject, the results of which will be published later.

Some confusion has arisen from the difference in standards of determination of prematurity. The diagnosis is customarily based on the weight of the infant, even though the length may permit a closer estimate of maturity. A weight of 5 pounds (2,268 Gm.) has been used by some authors as the upper limit of prematurity and of 5½ pounds (2,500 Gm.) by others. Data collected under these two standards are not strictly comparable. In the following reviews and tables, no attempt has been made to designate or to separate the results according to the standards employed, but in each case the author's diagnosis of prematurity has been accepted.

GENERAL ETIOLOGIC CLASSIFICATION

Hess [1] classified the causes of prematurity as follows:

(1) Expulsion of healthy premature infants, due to (*a*) injuries, falls or other types of physical exhaustion, (*b*) sudden emotional disturbances, (*c*) premature rupture of the membranes (accidental or

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1. Hess, J. H.: (*a*) Etiologic Factors Influencing Termination of Pregnancy, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 1, chap. 43, pp. 10-11; (*b*) Etiology of Prematurity, in Premature and Congenitally Diseased Infants, Philadelphia, Lea & Febiger, 1922, pp. 19-26; (*c*) Premature Infants, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 2, pp. 437-439.

intentional) and (*d*) nonobstetric surgical procedures; (2) conditions causing some damage to the offspring, for instance (*a*) constitutional disease of the parents, (*b*) chronic infections, such as syphilis, chronic nephritis, tuberculosis, heart disease and exophthalmic goiter, (*c*) acute infectious diseases, (*d*) local conditions, such as disease of the decidua or the endometrium, gonorrheal infection and malposition of the uterus, (*e*) anomalous positions of the fetus, (*f*) multiple pregnancy, (*g*) faulty nutrition of the fetus, caused by maternal fatigue, lack of sufficient food, wasting diseases, diabetes or blood dyscrasias, (*h*) intoxication by alcohol or heavy metals, (*i*) congenital malformations of the fetus, (*j*) advanced age of the parents, (*k*) frequent pregnancies, (*l*) habitual miscarriage and (*m*) seasonal influences.

The relative frequency of these various factors in a series of 844 cases of premature birth [2] was as follows: multiple pregnancy in 372 cases; toxic conditions of the mother in 131; chronic infections including syphilis in 109 and tuberculosis in 14; local pelvic abnormalities in 109; acute infections in 34, and other systemic diseases in 44.

Crawford's [3] review of causes of prematurity led to similar conclusions.

In a well controlled survey made by Woodbury [4] of a group of 1,158 premature infants in a series of 22,967 live infants born in eight cities during the years 1911 to 1916, prematurity was found to be unusually prevalent among (*a*) first-born infants, (*b*) infants of young mothers, (*c*) infants born in rapid succession, (*d*) children of mothers who had been gainfully employed during pregnancy, (*e*) infants of mothers who had multiple pregnancies and (*f*) boys. He concluded that the incidence of prematurity depends primarily on the health of the mother.

In a review of the histories of a group of 75 mothers of premature infants, Cook [5] found that 29 had had serious illnesses while the remainder had been entirely well or had had minor inconveniences, such as nausea and headache, which are commonly associated with pregnancy and which were not so abnormal that they should have had any effect on the children.

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2. Hess, J. H.; Mohr, G. J., and Bartelme, P. F.: The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934, pp. 17-21.

3. Crawford, W. H.: Premature Infants, Arch. Pediat. **48**:293-302 (May) 1931.

4. Woodbury, R. M.: Causal Factors in Infant Mortality, Bureau Publication 142, United States Department of Labor, Children's Bureau, 1925.

5. Cook, P.: A Clinical Study of the Premature Infant, Arch. Pediat. **38**: 201-216 (April) 1921.

Löfqvist's [6] investigation, conducted in Lund, Sweden, indicated that prematurity occurred most frequently in the infants of primiparas, especially if they were of advanced age. In a comparison of the incidence of certain conditions in the mothers of premature and in those of full term infants, little or no etiologic significance could be placed on hydramnios, oligohydramnios, ectopic pregnancy, placenta praevia, nephropathy, eclampsia, premature separation of the placenta, acute infections, tuberculosis or syphilis; but fetal malpositions, premature rupture of the membranes and anomalies of the cord occurred more frequently in premature than in full term pregnancies. A febrile puerperium and a higher total morbidity rate were noted more frequently for the mothers of the premature group.

ANALYSIS OF INDIVIDUAL CAUSES

Multiple Births.—This has been considered an important cause of prematurity by many authors. Table 1 indicates that this condition was responsible for 6.3 to 22.9 per cent of premature births in various series reported.

Toxemia.—This has also played a significant role in causing prematurity. In this summary, the term includes conditions reported as toxemia, eclampsia, preeclampsia or nephritic toxemia; it accounted for 1.4 to 29.9 per cent of premature births in the different groups.

Maternal Illnesses of Other Types.—Various conditions have been reported as causes of premature deliveries. The importance ascribed to syphilis has varied greatly in reports of different investigations. Jaeger,[7] Ylppö [8] and Israel and Kemkes [9] stated the belief that it is less of a factor today than in former years. Schoedel [10] stated that syphilis was of less importance than multiple pregnancies and abnormal positions of the uterus as a cause of prematurity.

Bleeding.—Hemorrhage resulting from placenta praevia, premature separation of the placenta or unstated causes has occurred with varying frequency in mothers of premature infants.

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6. Löfqvist, E.: Klinisch-statistische Untersuchungen über Frühgeburten, Acta obst. et gynec. Scandinav. (supp. 2) **11**:1-161, 1931; abstracted, Zentralbl. f. d. ges. Kinderh. **26**:358, 1932.

7. Jaeger, F.: Frühgeburt, Frühsterblichkeit, Schwangerenfürsorge, Monatschr. f. Geburtsh. u. Gynäk. **91**:191-213 (June) 1932.

8. Ylppö, A.: Zur Physiologie, Klinik und zum Schicksal der Frühgeborenen, Ztschr. f. Kinderh. **24**:1-110, 1920.

9. Israel, A., and Kemkes, B.; Statistische Beiträge zur Frage der Frühgeburten, Monatschr. f. Kinderh. **35**:289-302, 1927.

10. Schoedel, J.: Zum Frühgeburtenproblem, Monatschr. f. Kinderh. **53**: 349-360, 1932.

TABLE 1.—*Percentage of Incidence of Various Factors Which May Influence Prematurity*

Author	Number of Cases	Multiple Births	Toxemia	Syphilis	Serious Illness of Mother: Heart Disease	Serious Illness of Mother: Tuberculosis	Serious Illness of Mother: Other Acute and Chronic Conditions	Bleeding: Placenta Praevia	Bleeding: Premature Separation of Placenta	Bleeding: Unstated Cause	Abnormalities of Genital Tract: Pelvic Deformities	Abnormalities of Genital Tract: Myoma	Abnormalities of Genital Tract: Hydramnios	Premature Rupture of Membranes	Trauma to Mother	Other Conditions	No Cause Suggested
Brown, A.: Arch. Pediat. **34**: 609-616 (Aug.) 1917	68	....	20.6	3.0	...	...	8.8	1.5	...	....	...	...	...	....	...	1.5	64.7
Cook [5]	77	....	10.4	6.5	2.6	3.9	10.4	...	...	18.2	...	...	...	....	5.2	...	42.9
Milio, G.: Pediatria **38**: 809-827 (Aug. 1) 1930	129	16.3	20.2	11.6	3.9	1.6	8.6	15.5		....	...	0.8	0.8	....	...	...	20.9
Rapisardi, S.: Pediatria **39**: 748-765 (July 15) 1931	133	15.8	17.3	12.0	8.3	1.5	4.5	16.5		....	...	...	3.8	....	...	1.5	18.8
Crawford [8]	231	10.8	5.2	19.0	0.9	0.4	1.7	2.2	1.3	....	...	...	...	....	0.4	2.2	60.6
Murphy and Bowman [13]	238	6.3	11.8	8.8	1.7	0.4	3.4	2.9	5.0	....	2.9	0.8	0.4	0.4	...	2.9	53.4
Dunham, E. C., and McAlenney, P. F., Jr.: J. Pediat. **9**: 717-727 (Dec.) 1936	244	9.4	29.9	2.9	1.6	0.4	10.3	1.6	3.3	6.6	7.8	0.4	2.9	20.9	...	...	30.7
Ingram, C. H., Jr.: Am. J. Obst. & Gynec. **33**: 80-84 (Jan.) 1937	349	21.5	9.7	....	...	...	....	...	...	7.2	...	...	...	16.0	...	...	45.6
Waddell, W. W., Jr.; Purcell, C. W., and Wray, W. S.: South. M. J. **30**: 535-545 (May) 1937	422	17.1	28.2	2.8	0.5	...	6.5	4.4	2.5	1.2	0.9	0.5	1.2	1.4	0.9	1.2	34.2
Capper [14]	437	15.1	1.4	3.0	...	5.5	3.9	...	...	3.4	...	...	...	....	1.8	5.7	60.2
Tyson, R. M.: New York State J. Med. **34**: 811-817 (Sept. 15) 1934	469	10.7	12.8	18.8	1.9	0.2	2.8	1.9	5.1	....	...	0.6	0.9	....	2.1	...	41.8
Watton, W. F.: J. Pediat. **8**: 110-122 (Jan.) 1936	564	8.7	21.3	1.4	1.8	...	1.4	...	...	6.7	...	1.6	1.8	1.4	...	4.3	49.6
Fels and Sandberg [11]	662	13.1	4.8	8.9	0.9	1.5	7.9	5.0	0.2	1.4	5.3	0.3	0.2	2.9	3.8	9.8	36.2
Ylppö [3]	668	21.0	3.1	3.9	...	1.8	5.4	1.3	...	....	0.3	1.2	...	4.5	...	1.8	55.2
Israel and Kemkes [9]	902	11.0	1.5	4.8	0.1	1.4	2.6	1.3	...	....	0.3	...	...	....	0.1	...	76.9
Breese, B. B.: J. Pediat. **12**: 648-663 (May) 1938	987	16.2	17.5	1.7	1.0	0.4	2.0	4.0	1.6	2.0	...	...	1.8	10.2	...	5.2	43.0
Hess, footnotes 1 and 23; Hess, Mohr and Bartelme [2]	1,623	22.9	8.1	6.7	1.2	0.9	4.1	2.3	...	....	...	0.1	0.1	....	1.6	4.0	48.0
Peckham [15]	4,055	11.8	16.3	16.1	2.1	...	...	2.5	2.0	....	...	...	...	20.2	...	1.1	27.9
Stork: Arch. f. Kinderh. **99**: 109-118, 1933	...	....	10.0	5.0	...	...	....	9.0	...	....	...	...	...	....	2.0	...	74.0
Clifford [24]	958	....	28.0	....	...	...	4.0	5.0	...	7.0	...	...	...	....	...	...	....
Smith, T. C.; Andrews, H. S., and Limper, M.: Kentucky M. J. **30**: 551-559 (Oct.) 1932	538	....	15.8	....	...	...	....	...	...	....	...	...	...	....	...	...	....
Woodbury [4]	1,158	10.5	....	....	...	...	....	...	...	....	...	...	...	....	...	...	....
Jaeger [7]	222	9.9	....	...	...	...	....	...	...	....	...	...	...	....	...	...	....
Brander [17]	376	....	....	....	...	...	....	...	...	....	...	...	...	....	...	...	50.5
Beitz, quoted by Fels and Sandberg [11]	...	....	....	....	...	...	....	...	...	....	...	...	...	....	...	...	66.0
Wiegel, cited by Fels and Sandberg [11]	...	....	....	....	...	...	....	...	...	....	...	...	...	....	...	...	73.9
Bakker, cited by Fels and Sandberg [11]	...	....	....	....	...	...	...	...	...	....	...	...	...	....	...	...	92.8

Local Abnormalities of the Genital Tract, Premature Rupture of the Membranes and Traumatic Maternal Injuries.—These conditions have been reported by the various authors, but generally the frequency was low.

Maternal Age.—Fels and Sandberg [11] and Murphy and Bowman,[12] who compared the ages of mothers of premature infants in cases in which no other cause of the prematurity could be found with the ages of a series of mothers giving birth to infants of normal weight, found a predominance of young mothers among those giving birth to premature infants. These reports and others have been listed in table 2.

Order of Birth.—This seems to be an important factor. In the controlled studies of Woodbury [4] and Peckham,[13] prematurity occurred

TABLE 2.—*Percentage of Incidence of Premature and Full Term Births According to Maternal Age*

Author	No. of Cases	Maternal Age, Yr. 15-19	20-24	25-29	30-34	35-39	40-44
Premature births							
Murphy and Bowman [12]	80	27.5	27.5	20.0	15.0	8.75	1.25
Jaeger [7]	222	9.5	29.3	29.7	20.3	9.0	2.3
Fels and Sandberg [11]	662	14.6	42.4	23.0	11.5	6.2	3.4
Breese, B. B.: J. Pediat. **12**: 648-663 (May) 1938	964	12.0	31.0	23.0	17.3	12.7	3.9
Woodbury [4]	1,157	11.8	31.8	27.1	15.7	9.5	4.0
Peckham [13]	4,055	37.7	29.5	13.9	9.3	7.4	2.2
Tyson, R. M.: New York State J. Med. **34**: 811-817 (Sept. 15) 1934	450	25.1	50.9			24.0	
Full term births							
Murphy and Bowman [12]	80	11.4	32.9	26.6	16.5	11.4	1.3
Fels and Sandberg [11]	1,000	10.9	37.9	26.4	12.7	7.1	3.4
Woodbury [4]	21,809	6.6	29.9	28.9	18.6	11.8	4.2
Peckham [13]	35,399	33.7	33.1	16.5	9.2	5.5	2.0

with greater frequency than would be expected among first-born infants. A summary of these and other data is given in table 3.

Season of the Year.—Hess [1b] stated that the incidence of prematurity is greatest during the colder months. Bivings [14] found that the number of premature births was greatest among the deliveries occurring in the

11. Fels, E., and Sandberg, H.: Zur Frequenz und Aetiologie der untergewichtig geborenen Kinder, Monatschr. f. Geburtsh. u. Gynäk. **100**:248-257 (Oct.) 1935.

12. Murphy, D. P., and Bowman, J. E.: Frequency and Causes of Premature Birth: Report of Two Hundred and Thirty-Eight Cases, Am. J. Obst. & Gynec. **24**:273-276 (Aug.) 1932.

13. Peckham, C. H.: Statistical Studies on Prematurity: I. The Incidence of Prematurity and the Effect of Certain Obstetric Factors, J. Pediat. **13**:474-483 (Oct.) 1938.

14. Bivings, L.: Preconceptional and Prenatal Influences Affecting the New-Born, J. A. M. A. **101**:1703-1705 (Nov. 25) 1933.

fall; that is, among deliveries of babies conceived in the winter. The seasonal distribution for his series of patients was as follows:

Season	Premature Births Per Thousand
Winter	86
Spring	108
Summer	86
Fall	133

Bivings sought for a possible relation between the rate of prematurity and the hours of sunshine:

Year	Hours of Sunshine	Premature Births Per Thousand
1930	2,830	109
1931	3,084	88
1932	2,630	113

TABLE 3.—*Percentage of Incidence of Premature and Full Term Births According to Parity*

Author	No. of Cases	Para I	II	III	IV	V	VI	>VI
Premature births								
Dunham, E. C., and McAlenney, P. F., Jr.: J. Pediat. **9**: 717-727 (Dec.) 1936	190	48.9	....	....	....	....	....	....
Crawford [3]	231	50.6	....	....	....	....	....	....
Fels and Sandberg [11]	662	60.0	....	....	....	....	....	....
Jaeger [7]	222	69.8	18.5	11.7	....	....	....	....
Capper [16]	388	52.3	20.6	11.1	5.7	4.1	2.3	3.9
Breese, B. B.: J. Pediat. **12**: 648-663 (May) 1938	951	43.5	24.5	12.4	5.5	4.4	2.7	6.8
Woodbury [4]	1,158	39.5	21.3	11.7	8.0	4.7	3.9	11.1
Peckham [13]	4,055	44.7	18.5	9.2	7.1	5.3	3.8	11.5
Tyson, R. M.: New York State J. Med. **34**: 811-817 (Sept. 15) 1934...	471	42.5	21.7	11.0	7.9	6.6	10.40	
Full term births								
Woodbury [4]	21,809	26.5	21.6	14.6	10.9	7.9	5.6	12.9
Peckham [13]	35,399	35.9	20.0	12.0	8.4	6.0	4.8	12.9

Sex.—A predominance of boys among a large series of premature infants was found by Woodbury,[4] but the sex differences in other studies have been less striking.

Hereditary Factors Producing Defective Ova.—These have been suggested by Grulee [15] and by Ylppö [8] as causes of prematurity.

Nonobstetric Surgical Procedure.—Such an operation has been observed as a cause of prematurity in a few cases.

Fetal Anomalies.—These have been reported as causes by Fels and Sandberg,[11] Hess, Mohr and Bartelme [2] and Ylppö.[8]

15. Grulee, C. G.: Fetal and Neonatal Mortality, J. Pediat. **3**:132-143 (July) 1933.

Habitual Prematurity.—This was believed to occur frequently by Murphy and Bowman,[12] who reported that 12 of their series of 44 multiparous mothers of premature infants had previously had short term pregnancies. Habitual miscarriage occurred in only 4.1 per cent of Capper's [16] series, in 2.8 per cent of that of Fels and Sandberg [11] and in only 0.6 per cent of that of Ylppö.[8] One third of Brander's [17] patients had previously had premature deliveries, and in 4 of these cases, in which some other cause of prematurity was also present, the mothers had been premature infants. In the entire group there was a greater tendency than normal for other members of the families of these mothers to have premature offspring.

Maternal Nutrition, Fatigue and Other Factors.—Toverud [18] stressed the important relation between maternal nutrition and prematurity. A decrease in the incidence of premature births occurred when the mother's nutrition was improved by adequate amounts of rest and food. The highest weight and the highest weight-length ratios occurred in his series in August, when the amount of sunlight was greatest. Improvement also occurred with increases of age and of parity of the mother. Hirsch [19] stated that strenous work during the latter part of pregnancy increases the number of prematurely born infants and of infants with a low birth weight. Jaeger [7] and Schoedel [10] were convinced that the type of occupation of the mother during pregnancy influenced the incidence of prematurity. Ferrara [20] found that the duration of the mother's vacation from outside work before delivery determined to some extent the birth weight of the infant. Schneider [21] showed that the number of premature births increased definitely in Germany during the World War (1914 to 1918), when women had to replace men in all kinds of work. Peller [22] stated that a good nutritional status of mothers during the latter part of pregnancy resulted in better development of newborn infants, diminution in the number of premature and stillborn infants and reduction of neonatal deaths. Schoedel [10] attributed the decline in the incidence of prematurity, from 14.15 per cent in 1920 to 8.77 per

16. Capper, A.: The Fate and Development of the Immature and of the Premature Child, Am. J. Dis. Child. **35**:262-288 (Feb.) 1928.

17. Brander, T.: Einige konstitutionelle Momente in der Aetiologie der Frühgeburt, Monatschr. f. Kinderh. **77**:11-22, 1939.

18. Toverud, K. U.: Nutritional Condition of New-Born Infants: Statistical Study, Am. J. Dis. Child. **46**:954-962 (Nov., pt. 1) 1933.

19. Hirsch, M.: Mutterschaftsfürsorge, Leipzig, Johann Ambrosius Barth, 1931; cited by Toverud.[18]

20. Ferrara, cited by Hirsch,[19] p. 74.

21. Schneider, cited by Hirsch,[19] p. 113.

22. Peller, cited by Hirsch,[19] p. 74.

cent in 1930, to the better nutrition of the mothers. In a survey of 902 premature infants born in the years 1914 to 1925, Israel and Kemkes [9] observed that the number of premature births doubled during the years 1918 and 1919, the percentage of increase being greater than that of the general birth rate. No explanation for this increase in prematurity could be found except possibly an increase in crime and social unrest.

Illegitimacy.—Toverud [18] found that prematurity was more frequent in cases of illegitimacy, which may have been related to the social status of the mothers. Crawford [8] found that 17.3 per cent of his group of premature infants were illegitimate, and Jaeger [7] observed twice this percentage (36.5 per cent) in his series. Adequate data regarding this factor are not available.

Prenatal Care.—Hess [23] emphasized the importance of prenatal care, and Toverud [18] found that increases of infants' birth weights occurred if two months of antenatal care were given to the mothers. Prematurity was reduced to a third of its former rate at Maternity Center Association in New York by means of intensive and systematic prenatal care. In Fels and Sandberg's [11] series, a change of incidence of prematurity from 10.5 per cent in 1925 to 6.4 per cent in 1932 seemed to be influenced by prenatal care. Clifford [24] applied a method of determining the maturity of the fetus from measurements of the diameters of the skull on roentgenograms. He emphasized the use of such a procedure in allowing ill mothers to carry their infants until the optimum time for delivery.

Unexplained Prematurity.—In many instances the search for a cause of prematurity has yielded negative results. According to the reports in the literature and in some cases according to computations of the figures presented, the relative frequency with which etiologic factors of the condition could not be ascertained has varied from 18.8 to 92.8 per cent (table 1).

SUMMARY

Of the many predisposing factors reported to be causes of prematurity, it is difficult to determine which are the more frequent. Some of the variations in the conclusions reported probably arise from differences in the social and environmental conditions of the groups studied. Greater emphasis must be placed on the results of studies which include large numbers of cases and have been adequately controlled.

23. Hess, J. H.: The Chicago City-Wide Plan for the Care of the Premature Infants, J. A. M. A. **107**:400-404 (Aug. 8) 1936.

24. Clifford, S. H.: Reduction of Premature Infant Mortality Through Determination of Fetal Size in Utero, J. A. M. A. **103**:1117-1121 (Oct. 13) 1934.

Conditions which appear to be frequently associated with the premature delivery of an infant are multiple pregnancies and maternal diseases, such as the toxemias of pregnancy and chronic infections. In a few instances prematurity results from local abnormalities and disease of the genital tract, from acute systemic infections or from trauma. Prematurity occurs somewhat more often in the births of infants of very young mothers and with first-born children. When the nutrition of mothers is impaired by frequent pregnancies in rapid succession, by insufficient food and rest or by the overstrain of continuous work of a gainful occupation, premature births appear to occur more often than when the mothers are normal. Other factors, such as season of the year, heredity and the sex of the infant, require more investigation in order that their relative importance as etiologic agents may be determined. The influence of endocrinopathies and of vitamin imbalances on prematurity are being studied more extensively at the present time.

Without doubt, many of the predisposing causes of early delivery of infants work in combination to impair the health and nutrition of the mothers. Further investigation of these causal relationships would be valuable.

News and Comment

GENERAL

National Association for Nursery Education.—The Biennial Conference of the National Association for Nursery Education will be held in New York from Oct. 25 to 28, 1939, at the Hotel Pennsylvania. The theme of the conference, "Nursery Education Today and Tomorrow," and the program in action will interest workers in all organized groups concerned with the welfare of young children.

American Board of Pediatrics.—The American Board of Pediatrics will hold examinations during 1940 as follows: on April 30 and May 1, in New York; before the meeting of Region III of the American Academy of Pediatrics (date indefinite), in Kansas City, Mo., and before the meeting of Region IV of the American Academy of Pediatrics (date indefinite), in Seattle.

DEATHS

Dr. John C. Baldwin, a pediatrician of Baltimore, died on July 3 of acute coronary occlusion.

Abstracts from Current Literature

Anatomy and Physiology

COORDINATION OF THE SUCKING CENTER AND THE RESPIRATORY CENTER IN THE HUMAN SUCKLING. A. PEIPER, Arch. f. d. ges. Physiol. **240**:312, 1938.

Peiper made simultaneous records of respiratory and sucking movements in the human infant. The basic rhythm of the respiratory center in sucklings is slower than that of the sucking center. On intake of food, the sucking movements are first associated with irregular respiration, diminished amplitude of the respiratory movements or even complete inhibition of respiration; eventually, the sucking center forces its rhythm on the respiratory center. Sometimes one observes an after-effect, the respiration continuing in the sucking rhythm after the sucking has ceased.

SPIEGEL, Philadelphia [ARCH. NEUROL. & PSYCHIAT.]

EMBRYONIC AND POSTEMBRYONIC DEVELOPMENT OF THE CORTEX. M. BOROVSKY, Arkh. biol. naouk. **47**:5, 1937.

Borovsky studied areas 4 and 6 of Brodman in brains from persons of various ages by the Nissl method. He found that up to the second month of extrauterine life the upper two thirds of the precentral gyrus consists of six layers. After the second month the fourth layer disappears. He saw the elements of the fourth layer to a lesser or greater extent in the lower third of the gyrus at all times during the extrauterine life.

Borovsky observed diminution in the size of the Cajal cells up to the third month after birth. This he ascribed to shriveling and degeneration of the cells. He observed that the pyramidization in the cortex ends first in the fifth, then in the fourth and finally in the second layer, where the process is completed at the end of the ninth year. He further observed in the second layer at different ages pyramidal cells which are much larger than any other cells in this region. They are usually located at the boundary of the first layer. He assumed that the heterotopic pyramids of the first layer are partially formed from these cells. Borovsky states that the increase in thickness of the cortex of the anterior central gyrus is four or five times greater during the last month of embryonic life than during extrauterine life. With the exception of the fifth and sixth layers, all other layers gain more during the tenth month of postembryonic life than they do from birth to the age of 43 years. Borovsky observed that the number of nerve cells in a unit of surface of the white matter does not decrease during the first five weeks of life and that it decreases slightly during the next six years. During the same period there is a considerable increase in the mass of white matter with partial death of some of the nerve elements. He believes that the constancy in number of the nerve cells can be explained only by a continuous restitution through migration of nerve cells during postembryonic life. He suggests that the source of the postembryonic migration is the embryonic islets in the walls of the lateral ventricles and in the white matter. He noted also that the cells of the white matter increase in size up to the fourth week of postembryonic life and then become somewhat smaller and show no further changes.

NOTKIN, Poughkeepsie, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

Biochemistry; Bacteriology, and Pathology

STABILITY AND ANTIGENICITY OF STAPHYLOCOCCIC TOXOID. J. S. KITCHING and L. N. FARRELL, J. Immunol. **34**:1 (Jan.) 1938.

Within certain limits the rate of detoxication of staphylococcic toxoid was inversely proportional to the amount of formaldehyde used. When detoxication occurred rapidly, owing to the use of large amounts of formaldehyde, there was a smaller drop in potency in terms of antitoxin-binding units and of antigenic response in rabbits.

Dilution did not affect the stability of staphylococcic toxoid. It was observed that dilution of the toxoid increased its antigenicity when it was injected intravenously. When given subcutaneously, however, the diluted material was not a better antigen but was at least as effective as unmodified toxoid.

FOTHERGILL, Boston.

AGGLUTINOGENS M AND N IN ANTHROPOID APES. A. S. WIENER, J. Immunol. **34**:11 (Jan.) 1938.

Wiener demonstrated that agglutinogens M and N were present in the blood of all chimpanzees examined. These agglutinogens were similar to but not identical with the human agglutinogens M and N. Agglutinogen M was present in the blood of gibbons, orang-utans and some species of lower monkeys. Resemblances between these agglutinogens in various bloods showed some degree of correlation with the positions of these animals in the evolutionary scale.

FOTHERGILL, Boston.

UREASE REACTION OF B. ABORTUS. M. ARAI, J. Orient. Med. **28**:1145 (June) 1938.

Arai studied the biochemical behavior of three strains of the causative agent of undulant fever. Brucella melitensis gave a marked and Brucella abortis Bang a weak urease reaction, whereas Brucella abortis suis gave a reaction of intermediate strength. On the basis of these findings he holds the urease reaction test to be superior to the customary hydrogen sulfide test for typing strains of Brucella.

KATO, Chicago.

Metabolism; Infant Feeding; Milk and Other Foods

MODERN DECLINE OF BREAST-FEEDING. J. C. SPENCE, Brit. M. J. **2**:729 (Oct. 8) 1938.

This problem is discussed from many angles and in all phases with the following conclusion:

"It appears that the incidence of breast-feeding is declining. The causes of this are our increasing indifference to the value of breast-feeding and a mismanagement of the mother in the early stages of lactation. The correction of the fault lies mainly in the hands of those who tend and advise the mother in and shortly after her lying-in. Big hospital wards and crowded child welfare centers do not provide an atmosphere which encourages breast-feeding. Better education of doctors and maternity nurses in the care of infants may help to correct the fault; and that the importance of this education is not sufficiently recognized is suggested by the recent authoritative order of the Ministry of Health that panel practitioners attending their refreshing postgraduate courses are not to receive instruction in diseases of infancy or childhood."

ROYSTER, University, Va.

SOME NUTRITIONAL PROBLEMS OF CHILDHOOD. L. G. PARSONS, Brit. M. J. **2**:930 (Nov. 5) 1938.

This is a discussion along the lines indicated in the title, dealing largely with celiac disease or, as the author is pleased to consider it, "coeliac rickets." The

article does not lend itself to abstracting. However, the trend is indicated by his brief conclusion:

"There are many other deficiencies of nutrition in coeliac disease, which time does not permit one to deal with, but I thought that an account of the work on liver and carbohydrate metabolism which was inspired by a study of coeliac disease, and of its applications in the treatment of nutritional states, might prove interesting."

ROYSTER, University, Va.

CERTAIN ASPECTS OF KETOSIS AND ACIDOSIS. A. B. CORKILL, M. J. Australia **1**:923 (May 28) 1938.

Seeking to explain the decrease in dextrose tolerance which usually accompanies ketosis, Corkill was able to show that the ketone bodies are not responsible for this phenomenon by finding the response to orally administered dextrose in a rabbit during an infusion of sodium acetoacetate solution identical to that during an infusion of physiologic solution of sodium chloride. Inasmuch as the anterior lobe of the pituitary gland facilitates neodextrogenesis and inasmuch as during starvation the body is forced to produce carbohydrate from its own protein and fat, it may be that the decreased dextrose tolerance found in the presence of an inadequate supply of carbohydrate is dependent to some extent on overactivity of the anterior lobe of the pituitary gland.

In regard to acidosis and anesthesia, in all the cases investigated by the author the ketosis found after operation could be attributed to deprivation of food demanded by the dietary treatment of the patient's condition rather than to the anesthetic agent. He could find no correlation between ketosis and postanesthetic vomiting, except that the latter, if continued, would lead eventually to ketosis. Concerning the relation of lactic acid to postanesthetic reduction in alkali reserve, a determination of the lactic acid in the blood immediately before the administration of the anesthetic showed high values (due to nervous excitement) whereas a determination at the end of the operation showed normal values. This finding seems to rule out the theory that the fall in plasma bicarbonate content is due to accumulation of lactic acid. There is some evidence that during anesthesia an unknown form of organic acid accumulates in the blood and is excreted in the urine. This acid is soluble in ether, and its accumulation might possibly account for the diminution in alkali reserve.

GONCE, Madison, Wis.

WHEN DOES ONE BEGIN ARTIFICIAL FEEDING IN BUDAPEST? J. BRINDLMEIER, Orvosi hetil. **82**:84 (Jan. 22) 1938.

The mothers of about 1,000 babies were interrogated, and it was learned that 84.67 per cent of their babies received mother's milk for one month, 76.44 per cent cent for two months, 57.38 per cent for three months and 30.84 per cent for five months. The situation in Germany is worse than in Budapest, for the data of Husler show that in Germany 32 per cent of the babies are breast fed for six to eight weeks, 40 to 50 per cent for three months and 8 to 10 per cent for six months. One can see that breast feeding is not lacking in Budapest, but nonetheless infant mortality is very high, 10.2 per cent. The cause of this high mortality is therefore to be sought in other factors.

GÖTTCHE, Budapest, Hungary.

ACUTE DEHYDRATION WITHOUT TOXIC SYMPTOMS. G. SURÁNYI and R. MARTYN, Orvosi hetil. **82**:126 (Feb. 5) 1938.

A 14 month old child was admitted to the pediatric clinic at Budapest with a body weight of 6,150 Gm. The child suffered from active vomiting diarrhea (without any trace of blood or pus in the stool) and high fever. No mental disturbance, toxic respiration or glycosuria was to be found. The child lost weight steadily

and died in six days. The pathologic examination showed hyperemia and swelling of the mucus membrane of the lower part of the duodenum and of the jejunum. The histologic picture showed necrosis of the superficial tissues in these parts of the mucus membrane. Thus the cause of this serious pathologic condition was an isolated inflammation of the small intestine. In spite of this many toxic symptoms were lacking.

GÖTTCHE, Budapest, Hungary.

BACTERIOLOGICAL OBSERVATIONS ON ACID MILK IN INNER MONGOLIA. Y. HONDA, J. Orient. Med. **28**:905 (May) 1938.

Acid milk is used only by certain tribes of Mongolians and by a small portion of the Russian population in Inner Mongolia. For the most part acid milk is prepared in wooden barrels, with occasional agitation by means of wooden sticks. Natural fermentation is the usual method, but artificial fermentation by addition of honey, starch or powdered bread is often resorted to.

Specimens of Mongolian acid milk from twelve different sources were cultured on nutrient agar medium containing 1 per cent dextrose and liver. The best results were obtained by culturing first anaerobically (40 to 50 mm. of mercury) and later aerobically. In these cultures 37 varieties of bacteria were differentiated and distributed as follows: 3 strains of rod-shaped bacteria, 2 types of cocci and 1 tetragenus. Two types of yeast fungi were found. All organisms gave a positive Gram reaction.

Both rods and cocci grew poorly in peptone water and ordinary bouillon medium, but fungi did better. Indol formation was absent in all cultures. No micro-organism formed gas in dextrose medium, but 25 per cent of the yeast fungi did. No reduction of neutral red was seen with any micro-organism, but 83 per cent of fungi yielded positive reduction. The micro-organisms produced hydrogen sulfide, but fungi gave diverse results. A hemolytic property on medium containing blood was not demonstrable. All the bacilli fermented dextrose and maltose; lactose was fermented by certain ones. In sugar fermentation tests the cocci gave varying results. The fungi consistently split levulose, dextrose and maltose but split galactose only occasionally. The bacilli and cocci showed catalase action, but the fungi showed none. With bacilli the acid tolerance was marked, but not so with cocci and fungi. According to Uffelmann, all these organisms are called acid milk bacilli. They are nonpathogenic to mice. After drying the fungi remained alive for three months, whereas the bacilli and cocci died in three minutes. In artificial gastric juice, diluted five times with water, both bacilli and cocci remained alive for twenty to thirty minutes, while the fungi lived more than forty minutes.

Such intestinal bacteria as Bacillus typhosus, Bacillus paratyphosus A and B and Bacillus coli communis were destroyed in two to three days after coming in contact with the micro-organisms of acid milk.

After being mixed with micro-organisms of acid milk, Brucella abortis Bang was destroyed in five days, the bovine type of Bacillus tuberculosis in ten days and the human type in four weeks.

KATO, Chicago.

Vitamins; Avitaminoses

EXPERIMENTAL RICKETS. G. S. DODDS and H. C. CAMERON, Am. J. Path. **14**:273, 1938.

Rickets was produced by the Steenbock-Block diet; healing was brought about mainly by administration of viosterol. Healing is described in detail from study of sections stained with hematoxylin and eosin, silver preparations and roentgenograms which were made frequently. The twelve roentgenologic stages of Bourdillon were used as a scale for measuring the progress of healing. The first

indication of healing was calcification in the rachitic metaphysis, close to the edge of the epiphysial cartilage, whence it spread, first through the metaphysis toward the shaft and later into the cartilage toward the end of the bone. The preliminary reorganization of the metaphysis involved provisional dilute calcification of the osteoid, calcification of the exposed cartilage trabeculae, increase in the amount of marrow and restoration of the marrow structure to normal. These changes restored the configuration of the trabeculae to what was almost normal by exposing the rather parallel cartilage trabeculae. The end of the shaft underwent much the same changes. At the same time the projecting cartilage masses became calcified and were partly removed, leaving calcified trabeculae very similar to those in the metaphysis. During the latter half of healing the shape of the bone became corrected; hematogenic marrow formed in the new end of the shaft, which had been formed from the metaphysial region; cupping was corrected, the entire epiphysial cartilage became normal in thickness and structure, and the reorganized trabeculae attained normal dense calcification.

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

HEMORRHAGE OF THE BRAIN AND RETINA IN SCURVY. E. SHAPIRO and S. HORWITZ, Arch. Pediat. **55**:327 (June) 1938.

Hemorrhage of the brain and retina is reported in a 6 month old girl with scurvy.

ORR, Buffalo.

EFFECT OF VITAMIN D ON CALCIUM AND PHOSPHORUS METABOLISM: STUDIES ON FOUR PATIENTS. F. ALBRIGHT and H. W. SULKOWITCH, J. Clin. Investigation **17**:305 (May) 1938.

Studies of calcium and phosphorus metabolism were made on 4 patients: a boy 4 years old, with a form of rickets resistant but not intractable to vitamin D therapy, and 3 young adults with idiopathic hypoparathyrodism. The relation of parathyroid activity to various sequelae of vitamin D therapy is discussed.

GUEST, Cincinnati.

A COMPARISON OF THE EFFECTS OF A. T. 10 (DIHYDROTACHYSTEROL) AND VITAMIN D ON CALCIUM AND PHOSPHORUS METABOLISM IN HYPOPARATHYROIDISM. F. ALBRIGHT, E. BLOOMBERG, T. DRAKE and H. W. SULKOWITCH, J. Clin. Investigation **17**:317 (May) 1938.

The action of dihydrotachysterol and of vitamin D on calcium and phosphorus metabolism was studied in 3 patients with hypoparathyroidism; in 1 patient the effect of parathyroid was also determined. Both vitamin D and dihydrotachysterol increased the absorption of calcium from the intestine and increased the excretion of phosphorus in the urine. The fact that dihydrotachysterol had a greater effect in increasing urinary excretion of phosphorus was thought possibly to explain why dihydrotachysterol is not antirachitic. The action of vitamin D was slower than that of dihydrotachysterol but lasted longer. The parathyroid resembled dihydrotachysterol in causing an increase in the urinary excretion of phosphorus but differed in that it probably had no primary action on the absorption of calcium from the intestine. Because of the similarity between the actions of parathyroid and dihydrotachysterol, the latter is an efficacious therapeutic agent in the treatment of hypoparathyroidism.

GUEST, Cincinnati.

ON THE ACTIONS OF CRYSTALLINE VITAMIN D_3 (CALCIFEROL) IN CHRONIC PARATHYROID TETANY. G. KLATSKIN, J. Clin. Investigation **17**:431 (July) 1938.

In 2 adults chronic parathyroid tetany which failed to respond to the usual therapeutic agents was satisfactorily controlled with calciferol (crystalline vitamin

D_2), with maintenance of the serum calcium and phosphorus at normal levels for periods of four and six months. The action of calciferol appeared to be dependent on an adequate intake of calcium.

GUEST, Cincinnati.

REQUIREMENTS FOR VITAMIN C IN MAN. M. HEINEMANN, J. Clin. Investigation **17**:671 (Sept.) 1938.

If a subject previously saturated with vitamin C is resaturated after having omitted all vitamin C for a certain length of time, the dose of ascorbic acid required to produce saturation corresponds to the quantity used from body stores during the vitamin C–free period. This amount divided by the number of days the experiment lasted can be considered as the daily expenditure. From the application of this test to a number of healthy and diseased subjects, the following conclusions were reached: At least 0.8 mg. of ascorbic acid per kilogram of body weight is used daily by healthy subjects saturated with this vitamin. Smaller amounts maintain a lower concentration in the body stores. To protect against scurvy, 0.4 mg. per kilogram or even less per day appears to be sufficient.

GUEST, Cincinnati.

ASCORBIC ACID AND COMPLEMENT FUNCTION. E. E. ECKER, L. PILLEMER, D. WERTHEIMER and H. GRADIS, J. Immunol. **34**:19 (Jan.) 1938.

These investigators have shown a correlation between the complementing activity and the ascorbic acid content of guinea pig serum. There was a fall in complement titer when the animals were kept on a scorbutogenic diet, and there was a rise in titer following the feeding of ascorbic acid. Ascorbic acid does not of itself act as complement in vitro. The authors suggest that the complementing activity of the serum of scorbutic guinea pigs and of patients may be used as a biologic indication of deficiency in vitamin C.

FOTHERGILL, Boston.

COMPLEMENTING ACTIVITY AND ASCORBIC ACID CONTENT OF GUINEA-PIG SERUMS FOLLOWING ETHER ANESTHESIA. E. E. ECKER, L. PILLEMER and D. WERTHEIMER, J. Immunol. **34**:39 (Jan.) 1938.

Ecker, Pillemer and Wertheimer pursued the observation that ether anesthesia increased the ascorbic acid content of the blood to determine whether a rise in complementing activity occurred also. No marked change in the complement titer of the serum of normal guinea pigs was noted following anesthesia, although a rise in ascorbic acid occurred. In animals fed a scorbutogenic diet there was only a slight rise in ascorbic acid content but a distinct rise in complement titer following anesthesia. In rabbits and rats, animals which synthesize their own ascorbic acid, no change in complement titer was observed following ether anesthesia.

FOTHERGILL, Boston.

EFFECT OF ASCORBIC ACID ON THE CONSTITUTION OF COMPLEMENT. E. E. ECKER, L. PILLEMER and D. WERTHEIMER, J. Immunol. **34**:45 (Jan.) 1938.

Ecker, Pillemer and Wertheimer studied the effect of ascorbic acid on the different components or fractions of complement. The recognized methods for fractioning complement were employed. Ascorbic acid had no reactivating effect on endpiece or midpiece. However, it produced increased action of reconstructed complement, i.e., a mixture of midpiece and endpiece. Ascorbic acid improved complement that was denatured by yeast. Heat-inactivated complement was not improved by the addition of ascorbic acid. The activity of complement reduced by aeration was markedly restored by the addition of this chemical.

FOTHERGILL, Boston.

ON RICKETS IN EGYPT. K. HULDSCHINSKY, Brit. J. Phys. Med. **1**:297 (Sept.) 1938.

Huldschinsky made a survey of the incidence of rickets in Egypt. His investigation included 240 children up to 12 years of age. His diagnoses were based on clinical signs for the most part. There were 104 children under 3 years of age. The incidence in children under 6 months was 20 per cent. The incidence in children from 6 months to 2 years of age was 65 to 75 per cent. He believes that the latter figures are more nearly correct because with the methods used it would be impossible to make the diagnosis for many of the small babies. He believes that the chief factors in the prevalence of rickets in Egypt are actinophobia, lack of education and exclusive breast feeding during the first year.

HARTMAN, Cleveland.

BARLOW'S DISEASE IN URUGUAY. R. C. NEGRO and A. MUNILLA, Arch. de pediat. d. Uruguay **9**:544 (Sept.) 1938.

Negro and Munilla claim that Barlow's disease is rare in Uruguay. In the last thirty-nine years only 30 cases have been reported. It occurs most frequently in dystrophic, artificially fed infants under 6 months of age. The diagnosis is confirmed by the history of the feeding and by the result of the therapeutic measures.

SCHLUTZ, Chicago.

CUTANEOUS LESIONS DUE TO VITAMIN A DEFICIENCY IN CHILDREN. A. CASTELLANOS and G. CONESA, Bol. Soc. cubana de pediat. **9**:402 (Sept.) 1937.

Castellanos and Conesa describe a case of vitamin A deficiency in which cutaneous lesions developed, which is the first case to be reported in Cuban literature. The lesion was a follicular hyperkeratosis without xerophthalmia. The use of a vitamin A preparation and a proper diet was followed by improvement within one month.

SCHLUTZ, Chicago.

EXPERIMENTAL INVESTIGATION ON THE RELATIONSHIP OF VITAMINS TO INFECTION. H. J. LAUBER, Beitr. z. klin. Chir. **164**:365, 1936.

In dogs with peritonitis good results were obtained with small amounts of vitamin A concentrate. Poor results were, however, obtained with overdosage. Vitamin C gave definite protection, and there was no effect with vitamins B_1 and D.

RUBIN, Boston.

TREATMENT OF SPASMOPHILIA WITH DIHYDROTACHYSTEROL. H. G. HUBER and B. BRAUER, Jahrb. f. Kinderh. **146**:265 (April) 1936.

The conclusion was reached that this particular preparation of dihydrotachysterol (A. T. 10), which was supposed to contain about 400 antirachitic units, was ineffective in the treatment of tetany.

LANDAU, Hannibal, Mo.

ASCORBIC ACID METABOLISM OF VERY SMALL CHILDREN AND THOSE OF SCHOOL AGE. F. WIDENBAUER, Jahrb. f. Kinderh. **146**:297 (May) 1936.

This study of the metabolism of ascorbic acid was made on infants and small children in Danzig, Germany. On considering the incidence of frank vitamin C deficiencies, the urinary excretion of vitamin C in health and disease and the results of attempts to demonstrate the Rumpel-Leede phenomenon, the authors concluded that vitamin C deficiency was infrequent.

LANDAU, Hannibal, Mo.

BLOOD TRANSFUSION AND RICKETS. J. WOLFF, Monatschr. f. Kinderh. **76**:30 (Oct.) 1939.

Wolff reports 5 cases of rickets in which the symptoms were relieved within seven to eighteen days by blood transfusions. The suggestion is that the citrated blood used contained various antibodies and vitamins. GERSTLEY, Chicago.

SHOCK TREATMENT OF RICKETS WITH VITAMIN D_2 AND D_3. H. J. HARTENSTEIN, Monatschr. f. Kinderh. **76**:163 (Nov.) 1938.

Hartenstein has previously shown that patients with rickets can be cured by one large dose of vitamin D. He now compares the efficiency of vitamin D_2 with that of vitamin D_3 as used in one single shock dose of 7.5 mg., given by mouth. Vitamin D_2 is obtained by irradiating ergosterol; vitamin D_3 from cholesterol. In a study of 24 patients vitamin D_3 proved definitely superior.

GERSTLEY, Chicago.

EFFECT OF VITAMIN C ON THE SCHICK REACTION. K. SCHWARTZER and L. STOCKEBRAND, Monatschr. f. Kinderh. **76**:197 (Nov.) 1938.

Twenty-one children for whom the Schick test was positive were given additional vitamin C. This therapy caused no diminution in their positive reaction.

GERSTLEY, Chicago.

EXPERIMENTAL SCURVY OF THE GUINEA PIG. M. GLASUNOW, Virchows Arch. f. path. Anat. **299**:120, 1937.

This lengthy contribution is divided into three parts: The first deals with age as a factor in the development of experimental scurvy in the guinea pig. The characteristic triad of changes in the teeth, abnormalities of bones and tendency toward hemorrhage occurs only in the young, growing animal. The scorbutic process appears to have a relation to the growth energy of the animal. In the adult guinea pig dental changes are most uniformly observed. In the guinea pig the teeth continue to grow throughout life. After bone growth has ceased, osteoporosis is usually the only change noted in the bones. The tendency to bleed may be very slight or entirely absent. The experimental scurvy of the adult guinea pig sheds light on some of the human osteopathies.

The second part of the paper presents the results of a study of the healing of the dental and osseous lesions. Under treatment these may heal so rapidly that all evidence of their occurrence may disappear within from thirty to forty days. New normal dentin is formed; the pathologic dentin is not organized. In the bones periosteal and endochondral ossification again become evident; callus forms at the sites of fracture; normal marrow is restored in the spongy bone, and abnormal and excessive bone is removed. The rapidity and completeness of the disappearance of the osseous defects bear a direct relationship to the dose of vitamin C.

The third section deals with the structural changes in the zone of endochondral bone growth. Study of the costal rosary of experimental scurvy leads to acceptance of the view that the cells of Ranvier's groove act as a cambium at the expense of which longitudinal growth of the costal cartilages occurs. The fibrous marrow forms an internal or endosteal callus, which undergoes no further differentiation. The osteoporosis of scurvy is the result of fibrous atrophy of bone. Scurvy is a disease of the entire mesenchyme, characterized by a loss of the property of differentiation on the part of the newly formed mesenchyme. The mode of action of vitamin C is unknown. O. T. SCHULTZ. [ARCH. PATH.]

VITAMIN C IN THE SPINAL FLUID DURING HUNGER. M. K. T. KASAHARA and M. HORIE, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:529 (Jan.) 1938.

The vitamin C content of the spinal fluid was studied in dogs, cats and monkeys. Dogs and cats are known to be able to synthesize their own vitamin C. In 8 dogs

the vitamin C content of the spinal fluid was determined before and after various periods (from three to twelve days) of absolute fasting. No alteration in the vitamin C content of the spinal fluid was found in any of the cats or dogs after fasting. Eight monkeys were studied in similar fashion after from two to twenty days of fasting. In monkeys there was a gradual decrease in the vitamin C content as the fasting continued. Just before death the vitamin C values were approximately one-fourth the normal figures.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

STUDIES ON HUNAN LOCAL FOOD PRODUCTS: I. THE CHEMICAL COMPOSITION AND VITAMIN C CONTENT OF HUNAN CITROUS FRUITS. T. F. SU and D. Y. LIU, Chinese M. J. **54**:40 (July) 1938. II. THE ANTISCORBUTIC ACTIVITY OF THE HUNAN KWANG CHÜ. T. F. SU and T. P. TU, ibid. **54**:44 (July) 1938.

Su and his co-workers publish the results of a comparison of oranges grown in China with those from California in point of vitamin C value. The province of Hunan was the first to cultivate oranges in China. In these studies analyses were made of the juice from five species of oranges and pemulos and the vitamin C determined by the quantitative method of Tillmans. Not only was the relative antiscorbutic acid content determined, but guinea pigs were fed the Chinese and the American fruit. The autopsies dealt with the effect of the respective juices in preventing hemorrhagic lesions throughout the body. Photomicrographs of the teeth show the protection given when orange juice had been administered. The conclusions are that Chinese citrus fruits are rich in vitamin C content and are recommended for use because of their low price and convenience.

NEFF, Kansas City, Mo.

Hygiene; Growth and Nutrition; Public Health

NUTRITION OF THE PRE-SCHOOL CHILD. V. SCANTELBURY, M. J. Australia **2**:148 (July 30) 1938.

Different types of inquiry are advised in making nutritional surveys of children none of which is entirely satisfactory. One type aims at rapid classification according to physical appearance, weight, height and the results of simple clinical examination. Another type involves a more thorough examination, which includes, in addition to the recording of data of the first type, an investigation of the economic and social status of the family, and also a series of laboratory tests to determine any predeficiency diseases. Still another type aims at learning the variations in the child's diet.

A survey under way now in Australia is making use of several different methods of study as follows: nine physical measurements are taken, so selected as to enable the following to be calculated: (1) height and weight for age, (2) weight for height, (3) arm-chest-hip index, and (4) the pelidisi index of von Pirquet.

According to the results of the physical measurements, the child is listed as "satisfactory" or "unsatisfactory." Those falling in the latter class are then submitted to one or other of the following: (1) a roentgen examination of the epiphyses at the wrist, (2) an estimation of the hemoglobin value, (3) Gothlin's capillary resistance test for scurvy and borderline scurvy, (4) a visual acuity test for partial night blindness.

In using height and weight tables it is important to realize that there are distinct differences in different countries, in different parts of the same country and in different social strata. It is therefore of greatest significance to make comparisons as to nutritional development by making repeated examinations at comparable times of the year. The use of some of the methods of analysis, such as the age-chest-height index, is complicated and requires considerable special training.

The results of the clinical examination in assessing nutrition are also subject to considerable variation. The author agrees with the statement by Dr. R. H. Simpson that "the opinion of a sound physician is still the best guide to the state

of nutrition." Nevertheless, examinations and attempts at classification are very useful. The things stressed by the author in physical examinations are pallor, posture, appearance of the median furrow of the back with the arms overhead, and the development of the skeleton as shown by such evidences in the bossing of the frontal and parietal bones, knock knees and enlargement of radial epiphyses. The condition of the teeth is considered important evidence of the state of nutrition. If it is important, the author feels that the Australian diet must be distinctly inferior since amazingly few children are found to have good teeth.

It is realized that somatometric and clinical findings show the morphologic state of the subject but that the malnutrition may interfere with the function before modifying form.

Attempts at making accurate determinations of the nutritional state are still unsatisfactory except for the few fairly definite tests for vitamin deficiencies.

The author concludes with a consideration of dietary charts and tables.

TENNEY, Madison, Wis.

SPECIAL METHOD OF MEASURING PHYSICAL DEVELOPMENT (THE "MINAHA" TRIANGLE). S. MIYAKE, S. MIYAKE, N. NAWA, S. HATTORI and H. YASUNAMI, Orient. J. Dis. Infants **23**:305 (March) 1938.

To facilitate studies of the physical development of growing children, the authors have devised a new method of body measurement, called the "Minaha" triangle. The base of this triangle is an imaginary line connecting the right and left nipples (M and M), and the apex is at the center of the umbilicus (N). By measuring this triangle in 775 school children, 99 newborn infants and 20 men the authors have found that in males both MM and MN are greater than in females. These values increase with advance in age, but the values become stationary for about a year, namely, between 9 and 10 years in boys and between 8 and 9 years in girls. In boys under 8 years and in girls under 9 years the MN value increases rapidly, whereas the MM value shows a great increase in adolescent males. The angle MNM measures 40 degrees in school children, the minimum being 39.5 degrees in male children during the eighth year and 38.94 degrees in female children during the seventh year. This angle is 46 degrees in newborn infants, while in adults it is 45.5 degrees. KATO, Chicago.

DEATH RATE IN CHILDREN ONE TO FOUR YEARS OLD IN NETHERLANDS. E. GORTER, Maandschr. v. kindergeneesk. **8**:69 (Nov.) 1938.

Gorter compares the death rate of children aged 1 to 4 years during the period from 1927 to 1931 with that during the period from 1932 to 1936. The mortality during the more recent period was one-third lower than that during the former period. The number of children dying of infectious diseases and acute diseases of the respiratory tract has been reduced 50 per cent, whereas for some diseases—for instance, measles—the diminution has been still larger. The number of children dying as a consequence of accidents has remained about the same.

VAN CREVELD, Amsterdam, Netherlands.

Prematurity and Congenital Deformities

DOES ANIMAL EXPERIMENTATION SHOW SIMILAR CHANGES IN THE EAR OF MOTHER AND FETUS AFTER THE INGESTION OF QUININE BY THE MOTHER? H. P. MOSHER, Laryngoscope **48**:361 (June) 1938.

In experiments on animals Mosher found that quinine, sodium salicylate and mapharsen fed to the mother or injected caused hemorrhages in the cochlea of the fetus. Eleven pregnant guinea pigs were given quinine in varying doses over varying periods, and 21 fetuses from these mothers were examined; 3 pregnant pigs were given sodium salicylate; and 7 fetuses were obtained for examination; 1 pregnant pig was given mapharsen, and 2 fetuses were obtained and examined. Six adults were not given medication and were used for controls. In all, 54 animals

were studied, and 40 to 50 sections were cut from each temporal bone, mounted and examined in series.

The paper deals only with the subject of hemorrhage and only with the observations on the guinea pig. It is implied that similar observations could probably be made in man were like experimental conditions possible.

Quinine and salicylic acid produced similar changes in the internal ear of the mother and in that of the fetus, more marked in the latter, the initial effect being hemorrhage in any part of the cochlea, about the basilar artery and even in the medulla. Quinine produced in both adult pig and fetus intense congestion of the cerebral vessels and vessels of the cochlea, associated with hemorrhage. Hemorrhage was found in every location, most strikingly about the eighth nerve in the cochlea and modiolus, around the seventh nerve, around the basilar artery, under the pia and in the medulla. Hemorrhage in the semicircular canals was rarely caused by quinine but was marked in the fetus whose mother had been treated with mapharsen. Sodium salicylate produced manifestations similar to those of quinine but less congestion of the vessels of the cochlea. The results of treatment with mapharsen were most striking. The cochlea of the mother might have passed for normal. The fetuses showed large hemorrhages in the scala vestibuli and vestibule, with abundant hemorrhage in the semicircular canals. All vessels were greatly dilated. Of the three drugs, mapharsen caused the most extensive hemorrhages in the fetus, though the cochlea of the mother showed no hemorrhage. The hemorrhages of the fetus were in the scala vestibuli, vestibule and semicircular canals and were extensive. In the animals treated with quinine and sodium salicylate the hemorrhages were practically always in the scala tympani and were about the same in both.

Mosher concludes that certain drugs pass from mother to fetus and produce similar changes in both. The effects on man are probably similar to those on animals.

Thirty-two photomicrographs illustrate the article.

WOOD, Newark, N. J. [ARCH. OTOLARYNG.]

GARGOYLISM. G. SLOT and G. L. BURGESS, Proc. Roy. Soc. Med. **31**:1113 (July) 1938.

Gargoylism is reported in a girl aged 6 years. The results of the physical examination and of the roentgen examination of the skull and of all the long bones are given in full.

WILLIAMSON, New Orleans.

GENETICS OF TRANSPOSITION OF THE VISCERA. E. A. COCKAYNE, Quart. J. Med. **7**:479 (July) 1938.

Transposition of the viscera is discussed from the genetic point of view. Cockayne states that complete transposition of the viscera is inherited as a recessive and is determined by a single autosomal gene. Its familial incidence and general distribution within a family, its occurrence in both members of a pair of monozygotic twins and the high percentage of first cousin marriages that give rise to it are all cited as proof of the foregoing statement.

An exceptional case of monozygotic twins, one normal and the other with transposed viscera, is referred to. Cockayne states that either somotic mutation or the loss of an autosomal chromosome would explain this situation.

BRADFORD, Rochester, N. Y.

FIFTEEN YEARS OF WORK OF A POLISH COMMITTEE ON CHILD CARE AND SCIENTIFIC PUBLICATIONS. B. KRAKOWSKI, Zycie Mlodych **7**:74 (March-April) 1938.

This volume is devoted to what has been accomplished along the lines of children's care and what needs to be accomplished along these lines. The following

men have expressed their thoughts: J. C. Babick, Helena Radlinska, Dr. Matylda Biehler, Dr. Zofie Gorlicka, Dr. Marceli Growski, Dr. M. Grzegorzewska, Prof. A. Janowski, Prof. K. Jonscher, Dr. T. Kopec, Prof. M. Michalowicz, Dr. T. Mogilnicki, Dr. S. Stankiewicz, Prof. W. Szenajch, Prof. J. Szmurlo.

KRUPINSKI, Chicago.

Newborn

COMPLEMENTAL FEEDING AND CARE OF THE SKIN IN THE NEWBORN. F. C. RODDA and A. V. STOESSER, Wisconsin M. J. **37**:547 (July) 1938.

A study of several groups of normal newborn infants (158 in a private hospital, 100 in a municipal hospital and 120 in the University of Minnesota Hospital) was made to determine the merits of starting complementary feeding during the first few days of life, as compared with offering water and breast milk only, unless after the sixth day the breast milk proved insufficient.

Standards for the groups compared were formulated and carefully followed. Only normal infants were included.

The average weight loss by the fourth day was between 5 and 6 per cent for both groups, and by the tenth day there was a definite gain in those not offered complemental feeding.

In the municipal hospital, where for several years there had been the rigid routine of offering infants water only until a definite breast supply had been established or its inadequacy demonstrated, 92.2 per cent were entirely breast fed on discharge and 7.8 per cent were getting mixed feeding. Of these, 86 per cent were still, at the end of the third month, getting breast feeding only.

It is concluded that early complemental feeding of the newborn does not lessen the initial weight loss and does not favorably affect the weight attained or the supply of breast milk as noted at the tenth day. It reduces the number of infants who are wholly breast fed on discharge from the hospital.

JANNEY, Wauwatosa, Wis.

HYDROPS FOETALIS (ERYTHROBLASTOSIS). V. BONNEY and H. J. S. MORTON, Proc. Roy. Soc. Med. **31**:1060 (July) 1938.

A young and healthy woman gave birth to her first child in 1934. It became jaundiced shortly after birth and died within forty-eight hours. A postmortem examination showed enlargement of the liver and spleen, and a diagnosis of infantile anemia was made. In 1935 a second child was born prematurely and was dead. It had been dead only a short time. Postmortem examination revealed fluid in all cavities of the body and great enlargement of the liver and spleen. This time the diagnosis was congenital syphilis, and in consequence the blood of the parents was examined, and in each instance the Wassermann reaction was negative. In 1937, being again pregnant, the mother came under the care of one of the authors (Morton). The blood was examined when she was six months pregnant, with negative results, and both the fetus and the uterus were of normal size, and the fetal heart was beating vigorously. The probability that the two previous deaths had been due to erythroblastosis was discussed, and it was decided to allow the pregnancy to continue a little longer and then deliver the child by cesarean section. In the meantime, however, the patient suddenly showed "heavy" albuminuria, edema of the face, legs and abdominal wall and acute enlargement of the uterus. The fetal heart could no longer be heard. Section was performed at once in the hope that the child might be alive. The child, which was dead, was about thirty-one weeks old and weighed 5 pounds 4 ounces (2,381 Gm.). All cavities contained a large quantity of port wine–colored fluid, and there were edema and slight hemolytic staining of all the organs and tissues. Blood from the heart showed a variety of nucleated forms, the most conspicuous being hemocytoblasts,

primary erythroblasts and megaloblasts. The placenta was enormous. It and the fetus were sent to the Bernhard Bacon Institute of Pathology, and the pathologist in charge (Gilmour) reported that no spirochetes were present in the liver or adrenals and that the general appearance, both macroscopic and microscopic, was identical with that in 14 other cases he had observed of erythroblastosis foetalis. The diagnosis and treatment are discussed.

WILLIAMSON, New Orleans.

CEREBRAL SEQUELAE, AFTER NEONATAL JAUNDICE, ASCRIBED TO KERNICTERUS. C. E. FIELD, Proc. Roy. Soc. Med. **31**:1121 (July) 1938.

A child aged 1¾ years was admitted to the hospital with the complaint that he could not sit up. He was jaundiced at birth and was treated with four blood transfusions. He was discharged with urine free from bile and the van den Bergh reaction falling. He held his head up at six months, but he never sat up or talked. For two months before admission to the hospital he was restless and limp and refused his food. A full report is given of the results of the physical examination and of other investigations.

WILLIAMSON, New Orleans.

CEREBROSPINAL FLUID IN NORMAL NEWBORN INFANTS AND INFANTS WITH MENINGEAL HEMORRHAGE. B. TASSOVATZ, Bull. Soc. d'obst. et de gynéc. **23**:673 (Nov.) 1934.

Tassovatz reports a series of 104 cases of menipgeal hemorrhage in infants.

A successful puncture of the spinal canal may be performed in 95 per cent of normal infants. The fluid is clear, and 4 to 5 cc. may be withdrawn. The color of the fluid varies with the degree of physiologic icterus. The fluid usually shows 30 to 150 red blood cells per cubic millimeter, and the presence of these cells does not seem to be due to the trauma of the puncture; 10 to 30 white blood cells per cubic millimeter are commonly found, and of these 60 to 80 per cent are macrophages, and the remainder are nearly all lymphocytes. Albumin is present in amounts of 0.4 to 0.56 mg. per hundred cubic centimeters. A pellicle tends to form in the fluid on standing.

In edema of the meninges, which occurs in infants in the course of difficult labors and in premature infants in association with slight degrees of hemorrhage, the spinal fluid has the same general characteristics, but the albumin is increased to 60 to 70 mg. per hundred cubic centimeters in full term infants and to 90 to 100 mg. in premature infants. The less the albumin the better is the prognosis.

Meningeal hemorrhage is uncommon in full term infants, occurring in about 0.5 per cent of them, associated usually with obstetric trauma. In premature infants the mortality from hemorrhage was 70 per cent. Meningeal hemorrhage may be divided into three types—mild, with 800 to 2,000 red blood cells per cubic millimeter; moderate, with 5,000 to 10,000, and severe, with 20,000 or more. The changes which the bloody fluid undergoes in the process of clearing up are discussed. The aseptic reaction of the meninges to various degrees of hemorrhage is emphasized.

GLASER, Rochester, N. Y.

BRONCHOPULMONARY STAPHYLOCOCCIC INFECTION OF THE NEWBORN; SEROTHERAPY, THEN VACCINE THERAPY; CURE. J. CATHALA and P. DE FONT-RÉAULX, Bull. Soc. de pédiat. de Paris **36**:71 (Jan.) 1938.

A newborn boy showed signs of bronchopulmonary infection on the twelfth day of life. In repeated roentgenograms the lower half of the right side of the thorax showed a dense shadow which did not have the appearance of an abscess cavity. The child vomited a considerable amount of each feeding, even though feeding was changed a number of times. On the thirtieth day purulent material was emitted from the mouth. Smears and a culture of this

revealed Staphyloccus aureus. He was given subcutaneous injections of staphyloccus antitoxin and later of staphylococcus vaccine, and finally, after he had become quite anemic, a blood transfusion. He recovered. On the basis of this and other observations it is concluded that the prognosis for the young infant with staphylococcic infection of the lungs and pleura may be better than might be supposed.

BENJAMIN, Montreal, Canada.

UMBILICAL DISCHARGES IN THE INFANT. G. L. HALLEZ, Progrès méd., April 16, 1938, p. 573.

In spite of good technic in caring for the umbilical cord, persistent discharge may be present. This may be due to a nonsyphilitic ulcer at the base of the umbilicus which occasionally leads to hemorrhage or which may be a portal of entry for pathogenic organisms. Such ulcers respond with scar formation to silver nitrate or calcium chloride or antihemorrhagic serum. Another type of ulcer may be on a syphilitic basis. The granuloma also produces continuous discharge and may be destroyed by treatment with silver nitrate. A fourth condition may be a persistent omphalomesenteric duct, which calls for surgical measures.

LESLIE, Evanston, Ill.

TRAUMATIC SEPARATION OF THE UPPER EPIPHYSIS OF THE FEMUR: A TYPICAL BIRTH INJURY. R. PFEIFFER, Beitr. z. klin. Chir. **164**:18, 1936.

Traumatic separation of the upper epiphysis of the femur is an infrequent but typical occurrence. Pfeiffer collected the several cases recorded in the literature and added 3 more of his own, and discussed them. He presents the etiologic factors, clinical findings and roentgenograms in these 3 cases. He divides all the cases into two groups according to the degree of dislocation. It is possible to get an excellent reduction by greater separation of the fragments at the beginning, in order to prevent traumatic coxa vara.

RUBIN, Boston.

Acute Contagious Diseases

EXPERIMENTAL INFECTION OF MICE WITH HAEMOPHILUS PERTUSSIS. W. L. BRADFORD, Am. J. Path. **14**:377, 1938.

A characteristic lesion has been produced in the lungs of mice by intratracheal inoculation of suspension of recently isolated Haemophilus pertussis. It consists in interstitial pneumonia with appearance of an excess of mucoid exudate within the smaller bronchi and alveolar spaces. The lesion of the parenchyma is more conspicuous than that of the bronchial epithelium. Pure cultures of H. pertussis have been consistently obtained from the infected lungs of mice from ten to twenty days after inoculation. The total leukocyte count has been regularly increased, and extreme degrees of hyperleukocytosis have been observed occasionally.

FROM AUTHOR'S SUMMARY. [ARCH. PATH.]

A METHOD FOR THE CONCENTRATION OF POLIOMYELITIS VIRUS IN NASOPHARYNGEAL WASHINGS. J. R. PAUL, J. Bact. **35**:493 (May) 1938.

The virus of poliomyelitis is not readily isolated from the nasopharynx of a patient with this disease. Most attempts result in failure, although it is still a question whether the frequency of failure is due to rarity of the virus at this site or to unsatisfactory technic. In an effort to improve the technic of isolating the virus from the nasopharynx in clinical cases of poliomyelitis, Paul worked out a method in which the virus is added to and recovered from normal nasopharyngeal washings. The virus suspensions are frozen and dried without addition of any "protective" substance, but later normal monkey serum is added. Measured amounts (usually 9.4 cc.) of each of the virus dilutions in nasopharyngeal washings are first placed in 25 cc. tubes suitable for use with the Flosdorf-Mudd

apparatus, and to each of these tubes 0.6 cc. of normal monkey serum is added, thus bringing the volume to 10 cc. The material is then frozen in a bath containing solid carbon dioxide (dry ice) and the methyl ether of ethyleneglycol (methyl cellosolve) for thirty minutes. The tubes are then attached to the apparatus, the vacuum pump is started, and the evaporating process is allowed to proceed for a period of from four to six hours, or until the volume of frozen material in each tube appears to be not more or not much less than about 0.5 or 0.6 cc. The tubes are then detached and placed in warm water to determine whether the residual material (when melted) has reached the correct volume. With the volume of the concentrate at about 0.5 cc. in each tube, measured amounts of sterile distilled water are added cautiously to each container sufficient to bring the volume of concentrate up to exactly 1 cc. Each concentrate (with a volume of 1 cc.) represents a tenfold concentration in volume from the antecedent sample. The series of tubes containing the concentrates are generally allowed to stand in the ice box overnight in a stoppered container and on the following morning 0.5 cc. from each sample is injected intracerebrally into a monkey.

Cultures from these inoculums made on blood agar plates were always sterile for bacterial growth.

STOESSER, Minneapolis.

BACILLUS PARA-PERTUSSIS: A SPECIES RESEMBLING BOTH BACILLUS PERTUSSIS AND BACILLUS BRONCHISEPTICUS BUT IDENTICAL WITH NEITHER. G. ELDERING and P. KENDRICK, J. Bact. **35**:561 (June) 1938.

Eldering and Kendrick describe the isolation of 10 cultures forming a homogeneous group from 7 patients with whooping cough by the cough plate method. These cultures were studied for their morphologic, cultural and serologic characteristics and with respect to certain reactions in animals. While closely related antigenically to both Bacillus pertussis and Bacillus bronchisepticus, these cultures are identical with neither. Their significance in connection with whooping cough is not yet clear. For convenience of reference, the name Bacillus parapertussis is used for the organisms described.

STOESSER, Minneapolis.

DETECTION OF THE VIRUS OF POLIOMYELITIS IN THE NOSE AND THROAT AND GASTRO-INTESTINAL TRACT OF HUMANS AND MONKEYS. S. D. KRAMER, J. Bact. **36**:290 (Sept.) 1938.

Nasal washings and stools from 20 patients convalescent from poliomyelitis and nasal washings, scrapings and intestinal contents from 7 monkeys killed at the height of the experimental disease were studied. These materials were treated with ether and concentrated in vacuo. The concentrated materials were inoculated intracerebrally and intraperitoneally into normal monkeys. Animals presenting suggestive symptoms were put to death, and serial passages to second animals were made. Positive detections of the virus were conceded when the monkeys presented symptoms and histologic changes compatible with experimental poliomyelitis. Virus from human sources was detected in 4 instances and virus from a monkey in 1 instance. Of the human strains, the first was obtained from the feces of a child seven days after onset of illness; the second, from the nasal washings of a child five days after onset, and the third and fourth, from the same patient nine days after onset, from the nasopharynx and the feces. The single strain recovered from a monkey was obtained from the gastrointestinal tract.

STOESSER, Minneapolis.

CULTIVATION OF VACCINIA VIRUS WITH RETICULO-ENDOTHELIAL CELLS. J. W. BEARD and P. ROUS, J. Exper. Med. **67**:883, 1938.

The pathogenic activity of vaccinia virus is in large part suppressed when the virus is mixed with living Kupffer cells or clasmatocytes in the test tube and injected intradermally. This virus increases in quantity when introduced into such

cultures in vitro and survives in immediate association with these cells. No antiviral principle is elaborated by the Kupffer cells under such conditions.

FROM AUTHOR'S SUMMARY. [ARCH. PATH.]

AN EPIDEMIOLOGICAL STUDY OF POLIOMYELITIS IN THE DISTRICT OF COLUMBIA. C. C. DAUER, Pub. Health Rep. **54**:205 (Feb. 10) 1939.

In a study carried on from 1925 to 1937 Dauer investigated 231 cases of poliomyelitis in children under 13 years of age. From 90 to 95 per cent of the patients had some paralysis, and the remainder had, besides the clinical symptoms, an increase of cells in the spinal fluid. The whole series was studied from the standpoint of geographic location, and there is evidence that there may be some form of direct or indirect contact between patients or a common source of infection or both. In 2 instances the disease appeared in 2 members of the same family; in 2 instances it appeared in 2 persons in the same institution; in 2 instances it developed in different families in the same dwelling, and in 3 instances the disease was reported from adjoining houses.

SANFORD, Chicago.

SCARLET FEVER IMMUNIZATION AND TREATMENT. O. M. LAYTON, Wisconsin M. J. **37**:797 (Sept.) 1938.

The Dick test has proved to be a reliable index to a person's suceptibility to scarlet fever. The Dick method of immunization, properly carried out, gives adequate protection against scarlet fever. It does not seem scientific or right to quarantine a person who does not have the disease, a person who can be proved to be immune or a person who, if susceptible, can be promptly immunized.

Wisconsin continues to have 15,000 to 20,000 cases of scarlet fever a year, a challenge to the authorities to employ more effective measures. The Wisconsin State Board of Health has officially endorsed the Dick method of immunization as both effective and safe.

At the St. Agnes Hospital School of Nursing all student nurses, most of the Sisters and many private patients have been given the Dick test for a number of years. About 30 per cent were reactors and were immunized. After two to three years retests showed 98 per cent still negative to the Dick test, and no cases of scarlet fever had occurred. Ideally, immunizations should be done between the second and fourth year of life, and it is not a "schoolroom job" but should be individualized.

JANNEY, Wauwatosa, Wis.

SCARLET FEVER IMMUNIZATION. A. B. SCHWARTZ, Wisconsin M. J. **37**:802 (Sept.) 1938.

This paper consists of the verbatim opinions of 6 authorities on contagion given in answer to questions on controversial points in scarlet fever immunization and the use of the Dick test. Those quoted are Drs. Jean V. Cooke, Gladys Dick, Archibald Hoyne, William H. Park, Philip M. Stimson and John A. Toomey. In general, they felt that immunization against scarlet fever is an effective method of preventing scarlet fever, but that reactions to it are sufficiently severe to make it an unpopular procedure in private practice. The Dick test is a reliable guide to immunity, and some method should be used to change a positive reaction to a negative reaction in persons, such as nurses and attendants, likely to be in contact with the disease. In opposition to such a procedure, Dr. Cooke maintained that clinical scarlet fever is not a true disease but a toxic reaction to hemolytic streptococci and that no immunity can be produced by injections of toxin.

JANNEY, Wauwatosa, Wis.

SCARLET FEVER IMMUNIZATIONS IN A GROUP OF NURSES. R. C. FOSTER, Wisconsin M. J. **37**:804 (Sept.) 1938.

Histories, urinalyses and Dick tests were recorded for a group of 77 student nurses, after which 35 were immunized against scarlet fever on an individualized

plan. They were then retested, and the urinalyses were repeated. At the end of six months they were submitted to the Dick test again. On the first test 51 had positive reactions. Because of histories of allergy or of rheumatism 16 of these were not immunized. Those having markedly positive reactions were given smaller, but a greater number of, doses of toxin than the ones with mild reactions, the number of doses ranging from 6 to 12. The average total dose was 169,000 skin test doses. Twenty-eight completed the immunizations. In some the immunizations were discontinued because of reactions and in others because of intercurrent illness. One patient had acute nephritis believed due to the scarlet fever toxin. Two weeks after immunization of the 28 girls, 5 still had positive reactions to the Dick test. These were reduced to 1 at the end of six months. The author felt certain that reactions to the toxins could be anticipated and were severe in proportion to the intensity of the original Dick test.

JANNEY, Wauwatosa, Wis.

COMBINATION OF VACCINIA WITH ANTIVACCINIAL SERUM. M. H. SALAMAN, Brit. J. Exper. Path. **19**:192, 1938.

Suspensions of vaccinal elementary bodies treated with antivaccinal serum suffer a reduction of their titer of infectivity. This reduction persists after all free serum has been removed. The reduction of infectivity is not the result of agglutination of the elementary bodies. The results recorded are consistent with the hypothesis which has been advanced for other serum-virus systems, that under constant conditions a given quantity of antiserum inactivates a constant percentage of any dose of virus on which it acts.

FROM AUTHOR'S SUMMARY. [ARCH. PATH.]

TYPE-SPECIFIC BACTERIOPHAGES FOR CORYNEBACTERIUM DIPHTHERIAE. E. V. KEOGH, R. T. SIMMONS and G. ANDERSON, J. Path. & Bact. **46**:565, 1938.

The condition produced in the skin of the rabbit by the injection of live pneumococci is inhibited by the addition of type-specific antipneumococcus serum in sufficient quantity to the dose of bacteria injected. Antipneumococcus serum inhibits the growth of the bacteria when injected with them in sufficient quantity. A method is described which permits comparison of the effects of varying doses of two antipneumococcus serums on a constant dose of live culture in the skin of the same rabbit. The potency in international units obtained by this method approaches that found by the mouse protection test. The accuracy of comparing two serums intracutaneously in a single rabbit is equal to that of the mouse protection test when 200 mice are inoculated. The nature of the effect of antipneumococcus serum observed by the rabbit intracutaneous method is discussed. The two reactions described may be caused by qualitatively different properties of the serum.

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

OBSERVATIONS ON DIPHTHERIA AND THE BACTERIAL TYPES OF CORYNEBACTERIUM DIPHTHERIAE. W. WILSON and N. E. GOLDSWORTHY, M. J. Australia **2**:509 (Sept. 24) 1938.

Wilson and Goldsworthy report the examination of 223 strains of Corynebacterium diphtheriae isolated from 348 patients having clinical diphtheria. They discuss the relative merits of Löffler's and Clauberg's mediums for the recognition of Corynebacterium diphtheriae and of Clauberg's medium and of two kinds of blood agar for the determination of types. Types intermedius and gravis caused on the average more severe disease than type mitis.

GONCE, Madison, Wis.

SERUM THERAPY AND NEW FACTORS IN THE TREATMENT OF CEREBROSPINAL MENINGITIS. P. ARMAND-DELILLE, C. LESTOCQUOY, J. P. PAILLAS and R. TIFFENEAU, Ann. méd.-chir. **3**:78 (March) 1938.

The treatment of cerebrospinal meningitis by specific serum has decreased the mortality from 70 or 83 per cent to 15 or 30 per cent. Various factors determine the efficacy of the serum therapy—the age of the patient, the duration of the disease, the organism itself and the type of serum. The authors believe that monovalent serums are more effective than polyvalent serums. They employ intraspinal, intramuscular and subcutaneous methods of administration. They think that repeated spinal drainage is of value. Various drugs have been used in the treatment of meningitis, without much success. Recently, sulfanilamide has produced the best results in the treatment of meningitis in infants. The daily oral dose is 4 Gm. for adults, 2 Gm. for children and 1 Gm. for infants. The drug can be used subcutaneously in the presence of gastrointestinal disturbances and can also be injected intraspinally, from 5 to 30 cc. of an 0.8 per cent solution being used. As neither serotherapy nor chemotherapy is infallible, it seems advisable to combine the two methods in the treatment of cerebrospinal meningitis.

DE JONG, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

CHILDREN VACCINATED WITH ANTIVARIOLAR VACCINE CULTURED IN VITRO. R. MARTIN, J. VAN COSTENOBLE and A. DELAUNAY, Bull. Soc. de pédiat. de Paris **36**:25 (Jan.) 1938.

Two children who had been vaccinated with cultured vaccine by scarification nine days previously were presented to show the lesions at the height of the reaction. At first intradermal vaccination had been employed, but scarification gave good results. The vaccine had first been used dry and emulsified in physiologic solution of sodium chloride, but was now suspended in neutral glycerin. The advantages of cultured vaccine are listed as the fact that it is sterile and that the reactions obtained are milder and leave less scarring. The immunizing power of this vaccine is considered to be as good as that of calf vaccine, based on tests performed on rabbits.

BENJAMIN, Montreal, Canada.

PURULENT MENINGITIS DUE TO MENINGOCOCCUS IN AN INFANT, CURED BY COMBINED SEROTHERAPY AND CHEMOTHERAPY. B. WEILL-HALLÉ, COCHEMÉ and LAUTMANN, Bull. Soc. de pédiat. de Paris **36**:103 (Feb.) 1938.

Meningitis developed in a 9 month old boy who had a positive tuberculin test. Meningococci were found in the spinal fluid. He was treated with antimeningococcus serum, injected intrathecally and subcutaneously, as well as with sulfanilamide given orally. He recovered completely.

BENJAMIN, Montreal, Canada.

TREATMENT OF ERYSIPELAS IN INFANTS WITH SULFANILAMIDE. G. CARDELLE Y PENICHET, Arch. de med. inf. **8**:34 (March) 1939.

Sulfanilamide is a specific for erysipelas and has reduced the mortality from this streptococcic infection by from 50 to 80 per cent. No ill effects have been noted. The exact dosage has not been determined, but a child's tolerance for this drug is high.

SANFORD, Chicago.

HEMORRHAGIC VARICELLA IN AN INFANT. J. MIR, Bol. Soc. cubana de pediat. **10**:457 (Aug.) 1938.

Mir describes a case of hemorrhagic varicella in a 3 year old girl. A brother had simple varicella a few days previously.

The blood showed only slight leukocytosis. There were no evidences of hemorrhagic disease. The lesions were definitely diagnosed as due to a virus infection.

Two eruptions appeared at an interval of four days, starting first on the face and then on the trunk. The patient recovered and was left with very faint scars.

SCHLUTZ, Chicago.

WHOOPING COUGH VACCINE. A. STEEGER, Rev. chilena de pediat. **9**:592 (July) 1938.

Steeger states that whooping cough vaccine does not affect the course of the disease and should not be used in the treatment of patients, so as not to diminish its prestige, especially among the laity. He highly recommends its use as a prophylactic.

SCHLUTZ, Chicago.

Acute Infectious Diseases

EPIDEMIOLOGIC AND IMMUNOLOGIC EXPERIMENTS ON RABIES. L. T. WEBSTER, New England J. Med. **217**:687 (Oct. 28) 1937.

Rabies in dogs appears to be increasing in a relatively unpredictable manner, and more livestock is becoming infected.

Epidemiologic studies on the amount and distribution of rabies virus are being carried out with a mouse inoculation test devised in the laboratory of the Rockefeller Institute. Brain tissue from a subject suspected of having rabies is emulsified and injected into the brains of 6 Swiss mice. If the injected material contains rabies virus, these mice, following inoculation, show Negri bodies in their brains by the sixth day. By the seventh day they become paralyzed, and by the tenth day they nearly always succumb to rabies. Of about 400 consecutive specimens, those positive for Negri bodies were likewise positive with the mouse test, but of the remaining 200 specimens, reported negative for Negri bodies, 15 to 20 per cent proved positive with the mouse test.

Among large numbers of mice receiving injections of rabies virus an occasional one remains well or survives with paralyses, tremors or general malaise. Several months later, when killed, its brain may both harbor virus and show characteristic lesions. Leach, employing the mouse test on specimens from dogs with indefinite ailments, such as running fits, in whose brains no Negri bodies were found, has demonstrated rabies virus.

The mechanism of immunity to rabies and the value of present vaccines are under scrutiny. Neurotropic viruses are said to travel to the central nervous system by way of nerves, and once established in the nerve cell cannot be destroyed. In rabies this implies that once the virus reaches a nerve cell from the site of inoculation the treatment by vaccine becomes ineffective. Immunization against virus infections is regarded as possible only with vaccines that are virulent; on this basis, only virulent antirabic vaccines, such as Pasteur's or Hogyes', can be regarded as effective. These are the main arguments against treatment with present antirabic vaccines after exposure.

This question is now being studied in experiments on Swiss mice. Oddly enough, virus cannot be detected in the peripheral nerve until it has been demonstrated in the brain or cord.

Virulent vaccine, according to McKendrick, is four times more apt to be followed by postvaccinal paralysis and is no more effective in treating human beings than is a nonvirulent vaccine. Hence, in this country a preparation phenolized according to Semple's method of destroying virulence is more generally employed. No single-dose, phenolized, nonvirulent vaccine immunizes mice to the slightest degree. Vaccines in which virulence has been reduced by phenol are correspondingly less effective as immunizing agents.

Attention is called to a new and promising source of vaccine in tissue culture virus. Used in its virulent state, a single dose immunizes mice readily without

harm. Of 30 dogs thus far immunized, none have been harmed. There remains, however, the difficult task of reducing the virulence of this culture vaccine without destroying its immunizing power.

GENGENBACH, Denver.

EFFECT OF SULFANILAMIDE ON RHEUMATIC FEVER AND CHOREA. B. F. MASSELL and T. D. JONES, New England J. Med. **218**:876 (May 26) 1938.

Of the 58 patients given sulfanilamide, 31 (53 per cent) showed toxic reactions. The chief manifestations were rash and fever. The rash was pink or red and usually maculopapular. It occurred on all parts of the body. There was slight, if any, itching associated with it.

Occasionally the rectal temperature rose as high as 103 F. Fever frequently occurred unassociated with a rash and then was usually higher than fever which accompanied a rash. The toxic reactions occurred most frequently between the seventh and the twelfth day after the beginning of the drug therapy but were observed as early as the second and as late as the thirtieth day.

In 9 persons presenting such toxic reactions, the repeated administration of small doses caused development of a state of tolerance.

Patients ill with active rheumatic fever were particularly prone to the devlopment of severe febrile reactions. This fact, together with the lack of any observed beneficial results, makes the administration of sulfanilamide contraindicated in the presence of active rheumatic fever.

There were 7 patients with slight to moderate chorea who were given sulfanilamide. Except for the chorea none of these presented any clinical signs or laboratory evidence of active rheumatic fever. The therapy had no effect on the natural course of the chorea in any of these patients.

GENGENBACH, Denver.

RHEUMATIC INFECTION. A. D. KAISER, New York State J. Med. **38**:868 (June 1) 1938.

Evidence shows that vitamin C plays an important part in determining the resistance of children to infections of certain types. Children with rheumatism have a deficient amount of vitamin C in the urine. This is especially true with acute rheumatic infections and less so with quiescent rheumatism. The blood of rheumatic patients shows a somewhat lower level of vitamin C. While administration of adequate amounts of vitamin C will not prevent or cure rheumatism, there is some evidence that rheumatic patients have an increased need for vitamin C. Studies of vitamin C in the blood and urine do not show that vitamin C deficiency is a signficant etiologic factor in rheumatic infections. It is important to give adequate amounts of this vitamin regularly to all patients suffering from rheumatism.

AIKMAN, Rochester, N. Y.

TETANUS ANTITOXIN. H. W. LYALL and P. P. MURDICK, New York State J. Med. **38**:882 (June 1) 1938.

Of 1,000 persons treated with prophylactic injections of tetanus antitoxin, 15.2 per cent responded with generalized serum reactions. In 3.5 per cent the reactions occurred within twenty-four hours. Only one fourth of the reactions were severe, and in but 2 cases were they alarming. In general, the reactions tended to decrease with increase in potency of the antitoxin and coincident drop in the protein content of the prophylactic dose. There is a steady downward trend of general reactions in age groups up to 40. The higher percentages in the younger groups were probably due to previous administration of horse serum products, among which diphtheria toxin antitoxin played an important part in sensitizing persons to later injections of tetanus antitoxin.

AIKMAN, Rochester, N. Y.

THE RHEUMATIC PROBLEM IN GREAT BRITAIN. M. CAMPBELL, Brit. J. Phys. Med. **1**:194 (June) 1938.

Campbell estimates that rheumatic diseases cost Great Britain at least £30,000,000 a year. He emphasizes the need for a national scheme to control rheumatism, to be carried on as energetically as the present campaign against tuberculosis. A definite program is suggested.

HARTMAN, Cleveland.

THE STREPTOCOCCAL DISEASES. S. THOMSON, Edinburgh M. J. **45**:695 (Oct.) 1938.

This communication comes from the department of bacteriology of the University of Edinburgh. The discussion concerns scarlet fever, erysipelas, puerperal fever and the interrelationship of the streptococcic diseases. Thomson has correlated the occurrence of the streptococcic diseases in Edinburgh for the years 1931 to 1934 during which scarlet fever was epidemic. He believes that there is some relationship between the incidence of scarlet fever and erysipelas. He cites statistics at the Royal Hospital for Sick Children and has plotted a graph to illustrate this. He cites Lancefield's method of differentiating the various strains of hemolytic streptococci as showing that 80 per cent of acute infections in man are produced by type A. He has estimated the exotoxin recovered from a scarlatinal, an erysipelatous and a puerperal fever strain of hemolytic streptococcus. The strain from erysipelas gave the most potent exotoxin and the scarlatinal strain the next most potent. All three exotoxins were neutralized by the same antitoxin (of scarlet fever). Skin tests with the endotoxins produce no qualitative differences. Scarlet fever and ordinary streptococcic tonsillitis should be regarded as being epidemiologically identical, and it is noteworthy that public health administrators still fail to recognize this fact.

NEFF, Kansas City, Mo.

BACTEREMIA. J. A. RYLE, Lancet **2**:867 (Oct. 15) 1938.

Bacteremia, deriving often from trivial causes or alternatively accompanying a serious local infection, is more common than has generally been appreciated. Hemic infections may be clinically very innocent, moderately anxious or very serious. The nomenclature of hemic infections is unsatisfactory or at least requires review. Physicians must not allow such widespread perversions of judgment to prevail as prevailed in the case of the therapeutic vaccine craze. A plea is made for intimate cooperation between physician, pathologist and chemist.

LANGMANN, New York.

STAPHYLOCOCCIC ANATOXIN AND THE THERAPY OF STAPHYLOCOCCIC INFECTIONS IN GENERAL. G. RAMON, Arch. de méd. d. enf. **41**:665 (Nov.) 1938.

Up to the present time anatoxins have been employed only in the prevention of certain infections. As a result largely of the work of Burnet, a staphylococcic toxin, prepared after the usual method of preparing anatoxins, is now available in the management of such invasions. For the first time, therefore, anatoxin may be employed in the therapy of an infection during its evolution, as forecast by Ramon in his initial work. This observation has encouraged investigators to believe that similar contributions may be made to the treatment of diphtheria, as "sero-anitoxi-therapy."

A detailed discussion of the results in more than 1,000 cases of staphylococcic infections, with consideration of local and general reactions, is included, together with a review of numerous reports by clinicians in France, the French colonies, Belgium, Switzerland, England and the United States.

Various theories on the mechanism of anatoxin therapy are examined.

AMESSE, Denver.

TETANUS IN CHILDREN. E. SORREL, Bull. Soc. de pédiat. de Paris **36**:249 (April) 1938.

Tetanus developed in 3 children following minor superficial wounds. Two of the children died, one despite a prophylactic injection of tetanus antitoxin, and the third recovered. Sorrel discusses the advisability of immunizing all children against this disease. He recommends three injections of anatoxin, to be followed by another one when the child sustains any ordinary injury, and an injection of antitetanic serum as well if the wound is extensive.

BENJAMIN, Montreal, Canada.

SEROLOGIC REACTIONS IN SYPHILIS AND MALARIA IN INFANCY. A. SELLEK AZZI and A. DEL FRADE, Arch. de med. inf. **8**:388 (Sept.) 1938.

A correlative study was made on the blood of 20 infants with malaria (Plasmodium praecox found in 15 and Plasmodium vivax in 5) with the Kahn, Meinicke and the Sellek-Frade tests. Syphilis being excluded, the Kahn test gave 10 per cent, the Meinicke test 5 per cent and the Sellek-Frade test 5 per cent positive results. There is a difference of opinion in the literature as to whether persons with malaria will or will not give positive serologic reactions. The authors conclude by an analysis of their results that malaria (at least in infants) is capable of giving a low postitive reaction during an attack of fever.

SANFORD, Chicago.

RHEUMATIC INFECTION IN CHILDREN OF URUGUAY. D. CORREA, Arch. de pediat. d. Uruguay **9**:314 (Aug.) 1938.

The percentage of rheumatic infection as well as the mortality from this disease has increased during the past years in Uruguay. About 80 per cent of the children with rheumatic infection have not received treatment. Hence Correa claims that it is a medical and social problem calling for more intensive consideration.

SCHLUTZ, Chicago.

LARGE DOSES OF IRON IN THE TREATMENT OF TRICOCEPHALUS INFECTION. A. CASTELLA, A. PAUSSA and J. TRUJILLO, Bol. Soc. cubana de pediat. **9**:425 (Oct.) 1937.

It is known that iron salts alleviate the anemia resulting from parasitic infections. The authors have observed that on giving large doses of iron salts Tricocephalus disappears rapidly. Cases are presented in which improvement occurred.

Iron and ammonium citrate was the preparation chosen. Large doses were given orally and occasionally as enemas. The action is said to be due to the by-products of the decomposition of the preparation or to small amounts of the unchanged drug that reach the cecum and colon.

SCHLUTZ, Chicago.

TWO CASES OF TETANUS. G. GARCIA MONTES and others, Bol. Soc. cubana de pediat. **10**:530 (Sept.) 1938.

The authors present 2 cases of tetanus which are interesting from two points of view: the portal of entry (in one the virus was transmitted through the nasal cavity with a dirty piece of paper, and in the other it followed tonsillectomy) and the favorable course despite the cephalic portal of entry.

Treatment consisted in the administration of antitetanus serum, anesthetization with avertin with amylene hydrate (60 mg. per kilogram) and subsequent use of phenobarbital.

The authors believe that the portal of entry affects neither the prognosis nor the incubation period and that the toxin reaches the nervous system mainly by way of the blood stream and to a slight extent through the lymphatics around the wound.

SCHLUTZ, Chicago.

STATISTICAL STUDY OF INTESTINAL PARASITISM IN THE YEAR 1937. M. J. BORILARI and M. D. CASTELLINO, Rev. méd. latino-am. **28**:1159 (July) 1938.

Of 146 patients examined for intestinal parasites in Hospital Rawson in Argentina, 97 (66 per cent) were found infected and 49 (34 per cent) uninfected. The parasites more commonly found were Blastocystis hominis (75 times), Endamoeba coli (34 times), Endamoeba histolytica (24 times), Giardia intestinalis (17 times) and Trichomonas hominis (12 times). The helminths were relatively uncommon. The Trichocephalus dispar occurred 6 times and Taenia saginata 5 times in the total of 97 cases of parasitic infection.

DWYER, Kansas City, Mo.

Chronic Infectious Diseases

MAPHARSEN IN TREATMENT OF CONGENITAL SYPHILIS. V. A. CORNELL and G. D. ASTRACHAN, Arch. Dermat. & Syph. **38**:943 (Dec.) 1938.

The serologic and clinical effects of mapharsen were studied in 42 children with congenital syphilis. The claim of low toxicity for mapharsen was definitely confirmed. Some of the patients with early congenital syphilis were given intramuscular injections of mapharsen and showed no untoward reactions. The serologic effect is difficult to evaluate from the data given. The fact that patients with late congenital syphilis did not respond serologically to neoarsphenamine therapy and did improve with addition of mapharsen therapy is evidence that prolonged arsenical therapy is indicated in patients with the so-called fixed serologic reaction.

JACKSON, Iowa City.

DANGER OF PRIMARY ABDOMINAL TUBERCULOSIS IN CHILDREN. S. ENGEL, R. O. STERN and G. H. NEWNS, Brit. M. J. **2**:1038 (Nov. 19) 1938.

The authors discuss this danger, citing the incidence of primary abdominal tuberculosis and stating the criteria of a primary abdominal focus.

"Our diagnosis of 'primary abdominal infection' was based on enlargement with obvious tuberculous infection of the mesenteric lymph glands, with or without caseation, and complete absence of evidence of tuberculous infection of the bronchial or other mediastinal glands. No case was included in this series in which any enlargement whatsoever of the bronchial glands was recorded, or in which there were any tuberculous lesions of the lungs other than the miliary tubercles seen as a result of generalized dissemination of the disease."

After citing 3 cases, they come to the following conclusions:

"Primary abdominal tuberculosis is a commoner disease in children than is generally supposed, and the true incidence is much higher than post-mortem figures indicate.

"In primary abdominal infection, as in cases with a primary lung infection, the prognosis depends on the age of the child: the younger the child at the time of infection the worse the prognosis.

"We are unable to accept the current view that primary abdominal tuberculosis can be more lightly regarded in children than can a primary lung infection: the bad prognosis in young children refutes this view. Diagnosis in cases of primary abdominal tuberculosis in the living child is extremely difficult; consequently early treatment is rarely possible. Prevention of infection is therefore all-important. Many cases of tuberculous meningitis, miliary tuberculosis, and crippling deformities could be prevented. We should endeavor, as an ideal, to secure for children milk from tuberculin-tested herds only, but at present it is impossible to provide this for the whole population. Therefore the greatest measure of protection is afforded by milk which has been boiled or efficiently pasteurized."

ROYSTER, University, Va.

THE INTRACUTANEOUS TUBERCULIN TEST OF MANTOUX: A METHOD EMPLOYING A SINGLE INJECTION. D. ANDERSON and C. HARVEY, M. J. Australia **2**:378 (Sept. 3) 1938.

Using the standard test doses of Long, Aronson and Seibert, the authors employed 0.00002 mg. and 0.005 mg. of tuberculin (purified protein derivative) in 0.1 cc. of buffered saline solution to determine positive reactors. Feeling that severe reactions were too frequent and desiring a single test dose for use in surveys of large numbers of the population, they compared reactions to the second, or larger, dose of 0.005 mg. in 0.1 cc. of saline solution with the reactions to 0.00125 mg. of tuberculin (purified protein derivative) in 0.025 cc. of diluent. The first test dose, which is equal to 1 mg. of old tuberculin or 1 cc. of 1:1,000 solution, was injected intracutaneously into the right arm, and the second dose, equal to two and one-half times 0.1 cc. of 1:1,000 solution of old tuberculin, was injected into the left arm. This experiment was made in 123 volunteers, some of whom were known reactors. It was found that the second dose, which was one-quarter the volume of the standard strength second injection of tuberculin (purified protein derivative), detected all or nearly all positive reactors, that the specificity of the smaller reactions is still unmistakable to the experienced observer and that the sharper reactions are considerably less severe. After a series of 1,000 tests with the single dose the authors recommend its use in large surveys. However, when practicable the standard two test dose is recommended.

GONCE, Madison, Wis.

GENERAL PARALYSIS IN A MOTHER AND DAUGHTER. POROT, BARDENAT and SUTTER, Rev. neurol. **69**:190 (Feb.) 1938.

Dementia paralytica appeared in a girl of 11 years. Four years later this disease developed also in her mother, aged 47. The authors do not enter into any discussion of the cases.

DAFFINEE, Boston.

MOTH CERASE AND TUBERCLE BACILLI. HARRIEHAUSEN and STADLER, Monatschr. f. Kinderh. **75**:202 (Sept.) 1938.

The observation has been made that a certain type of moth is resistant to tuberculosis and that this may be due to cerase which destroys the fatty capsule of the tubercle bacillus. Harriehausen and Stadler prepared various extracts from the caterpillars but were unable to find any cerase in their preparations. They did, however, find an effect on the Ziehl-Neelsen stain. It was found that the acid-fast property ended after an exposure of from one hundred twenty to one hundred ninety hours to the caterpillar extract. Instead of the red-staining bacilli, only organisms colored steel blue were visible. In control specimens the tubercle bacilli remained one thousand hours without losing their acid-staining property.

The fact that this property was lost by exposing the mixtures to metals, disinfectants and heat suggests that the action is due to a ferment.

GERSTLEY, Chicago.

DEVELOPMENT OF TUBERCULOSIS OF THE CERVICAL LYMPH NODES. H. OPITZ, Monatschr. f. Kinderh. **75**:294 (Sept.) 1938.

Opitz was astonished at finding tubercle bacilli in the stomach washings of children with tuberculous cervical adenitis in the absence of any open pulmonary tuberculosis. In a clinical study combined with animal experimentation he was able to show that the tubercle bacilli could be obtained from the washings of the mouth and throat. He reports these observations as a preliminary study.

GERSTLEY, Chicago.

THE PATHOLOGIC NATURE OF TUBERCULOUS MENINGITIS. D. MÓRITZ and T. MESZNER, Orvosi hetil. **82**:240 (March 12) 1938.

Móritz and Meszner made extensive metabolic examinations of children with tuberculous meningitis and found that the most characteristic change is a lowering of the chlorine content in the blood. This is caused partly by great perspiration, partly by vomiting and partly by an inclination toward retention of water.

GÖTTCHE, Budapest, Hungary.

STUDIES ON THE FILTRABLE FORM OF TUBERLE BACILLI. Y. KIMURA, Orient. J. Dis. Infants **23**:32 (May) 1938.

Evidence in favor of the existence of a filtrable form of the tubercle bacillus is derived from the fact that when filtrates from cultures of human tubercle bacilli are grown in Kirchner's medium both acid-fast and nonacid-fast bacilli are obtained. Furthermore, if any of these same filtrates is injected into the subarachnoid space of the guinea-pig, the same results are obtained. On culturing the pia and the choroid plexus of the animal the microcultures of the nonacid-fast bacilli and the macrocultures are produced. The macroculture develops into the acid-fast form both in vitro and in vivo. The bacilli of both forms are polymorphic. The nonacid-fast bacilli after several passages through animals become acid-fast, but typical pathogenic bacilli of Koch's type cannot as yet be produced experimentally.

KATO, Chicago.

CULTURE OF TUBERCLE BACILLI IN STOMACH WASHINGS OF CHILDREN. K. MASE and S. SHINGU, Orient. J. Dis. Infants **23**:259 (March) 1938.

Stomach washings from 65 tuberculous children whose sputum had failed to disclose tubercle bacilli and from 6 nontuberculous patients as controls were cultured, after treatment with 5 per cent sulfuric acid, on two types of medium: Löwenstein's malachite green–asparagin–egg medium and Kirchner's liquid medium of rabbit serum. Positive results were obtained in cases of open tuberculosis, disseminating tuberculosis, miliary tuberculosis, primary infiltration, perifocal infiltration, pleuritis and erythema nodosum. Findings were negative in cases of pulmonary infiltration, epituberculosis, hilar gland tuberculosis and hilitis of Engel.

KATO, Chicago.

PHAGOCYTOSIS OF TUBERCLE BACILLI IN CHILDREN (OTANI'S METHOD). N. YAMAUCHI, Acta pædiat. japon. **44**:763 (May) 1938.

Applying Otani's technic of determining phagocytic phenomena to tubercle bacilli, Yamauchi found that type 2 of neutrophilic polymorphonuclear leukocytes (Arneth's hemogram) showed a higher percentage of phagocytosis as compared with type 3 leukocytes. The Mantoux reaction paralleled the percentage of phagocytosis.

KATO, Chicago.

MICROTEST OF SYPHILIS. M. PHILIPPI, Maandschr. v. kindergeneesk. **7**:450 (Aug.) 1938.

This is a description of experience with the microtest of Meinicke in 667 cases. A comparison with other tests gave results favorable to the Meinicke technic.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

ROLE OF COPPER IN IRON-DEFICIENCY ANAEMIA IN INFANCY. JAMES H. HUTCHISON, Quart. J. Med. **7**:397 (July) 1938.

From iron balance experiments performed on 9 infants suffering from nutritional anemia Hutchison concludes that "(*a*) the administration of copper enhances

the conversion into hemoglobin of iron stored in the tissues, (*b*) that iron given in doses so small as not materially to raise the hemoglobin content of the blood can, by subsequently giving copper, be mobilized and converted into hemoglobin." He suggests that copper, so administered, acts as a catalytic agent. The literature on the effect of copper in anemia due to iron deficiency is reviewed.

BRADFORD, Rochester, N. Y.

BLOOD TRANSFUSION IN INFANTS. H. VIAU, Union méd. du Canada **67**:170 (Feb.) 1938.

Viau describes his technic of using the lesser saphenous vein for blood transfusions in the case of infants. He discusses the advantages of the use of this vein over that of the longitudinal sinus, the external jugular vein, the median cephalic vein or the corpora cavernosa of the penis; he does not mention the use of veins of the scalp or the femoral vein.

DAFFINEE, Boston.

HAEMOLYTIC ANAEMIAS OF CHILDHOOD. L. G. PARTONS, Brit. M. J. **2**:851 (Oct. 22) 1938.

This is the Schorstein Memorial Lecture delivered at the London Hospital Medical College. It is based on observations of Partons and his colleagues in 120 cases. He thinks it inadvisable to divide anemia into primary and secondary and in fact has discarded this classification. He thinks that anemia is more of a symptom than a disease and that to give a proper name to an anemia is futile. Secondary anemia, he feels, is due in some instances to a deficiency of, or an inability to utilize, material for the manufacture of red cells and in other instances to loss of blood; it is possible for a given anemia to fall under both heads. Continued loss of blood, particularly in an adult, may lead to depletion of the iron stores in the body. The red cell passes through a series of changes following its formation in the marrow. However, in the hemolytic type of anemia reticulocytes form a conspicuous feature of the blood film, and their presence is not infrequently accompanied by an increase in the granular cells. There is a brief discussion on the erythronic response to injury. In this group Partons places acholuric jaundice, sicklemia, Cooley's anemia and hemoglobinemia. He considers erythroblastosis as hemolytic. Erythroblasts are normal in fetal life and early postnatal life. Sepsis or syphilis might produce a picture identical with icterus gravis at any time during the first fortnight of life. The degree of erythroblastosis depends on the degree of development of the extramedullary centers and in the opinion of Partons is a response to hemolysis and not a primary pathologic condition.

Von Jaksch's anemia is in many instances really a hemolytic anemia. It usually occurs in children under 3 years of age, is insidious and has a good prognosis. Sometime during illness there is leukocytosis. Von Jaksch never gave a clear account of the anemia. The syndrome occurs during the "deficiency age period," the time when scurvy or rickets occurs. It may occur during the course of icterus gravis and in children suffering from subacute hemolytic anemia. Von Jaksch's disease is not anemia at all, according to the author, but it merely presents a picture of erythroblastic anemia and occurs only during the "deficiency age period." Some cases are cited.

Sickle cell and Cooley's anemia are considered. Then follows a description of certain differences between acholuric jaundice and ordinary hemolytic anemia. He states that the hemolytic nature of sickle cell anemia cannot be denied. The bone changes are marked and more frequent than in acholuric jaundice. In this condition after puberty the spleen seems to atrophy.

In Cooley's anemia, which is almost entirely limited to children of Syrian, Italian or Greek stock, the bones of the skull and face produce a mongoloid appearance. The spleen is enlarged and often the liver and lymph glands, too. The cortex of the long bones is thin and transparent, and the medulla shows reticulation. Partons reports a case in which there was a combination of sickle cell and Cooley's

anemia. In elaborating on this case he thinks it is a case of one of the combinations of hemolytic and sickle cell anemia, although in this respect he is somewhat vague in his description.

ROYSTER, University, Va.

STENOSIS OF THE SPLENIC VEIN IN CHILDHOOD. J. HÖRA, Virchows Arch. f. path. Anat. **300**:670, 1937.

Thrombosis of the splenic vein in the adult leads to a characteristic triad of splenomegaly, gastric hemorrhage and secondary anemia, which permits clinical recognition of the condition. In children a somewhat similar complex of symptoms occurs, but operation or necropsy fails to reveal thrombosis or obstruction of the splenic vein. The noncommittal clinical term "stenosis of the splenic vein" has been applied to the condition in children. Failure to detect obstruction of the splenic vein has led to the supposition that the obstruction to the splenic circulation lies within the spleen itself. In children splenectomy usually leads to recovery; hence there are few records of observations made at necropsy. Höra presents a detailed histologic study of 2 spleens removed surgically, the first from a boy aged 8 years and the second from a girl aged 9 years. Neither grossly nor microscopically was there evidence of disease or of obstruction of veins outside the spleen. In each instance the spleen was enlarged to about four times the normal size. The splenomegaly was due to hyperplasia of the red pulp, with marked prominence of the sinusoids. Congestive hemorrhages had occurred in the trabeculae, and siderofibrous nodules had been formed, but there were no alterations within the spleen itself that would account for interference with the circulation through the spleen. The cause must be sought outside the spleen. In the absence of anatomic changes in the splenic vein one must consider functional stasis of the vein or obstruction of the portal circulation.

SCHULTZ, Chicago. [ARCH. PATH.]

CURABILITY OF GENUINE LOW BLOOD PRESSURE IN CHILDHOOD. G. SURÁNYI, Orvosi hetil. **82**:469 (May 14) 1938.

Forty-two children with genuine hypotony who were otherwise healthy were treated with various medicaments (ephedrine, strychnine, extracts of the posterior lobe of the pituitary gland) without success. A steady rising of the blood pressure occurred only in patients who came to puberty, but this was only a spontaneous rising.

GÖTTCHE, Budapest, Hungary.

ON BLOOD COAGULATION AND PROTEIN SPREADING. G. J. VAN LOOKEREN CAMPAGNE, Maandschr. v. kindergeneesk. **8**:5 (Oct.) 1938.

Blood coagulation was studied by means of the method of protein spreading introduced for such purposes by Gorter. The author is of the opinion that the preparation of pure prothrombin is at present practically impossible. He is inclined to accept the statement that the influence of calcium is founded on the formation of a compound with prothrombin and that probably there is no question of a catalytic influence. The action of thrombin on fibrinogen is that of a ferment, but the action of the ferment starts intravascularly. Quantitative determination of prothrombin is provisionally impossible; likewise, such determination of thrombokinase.

VAN CREVELD, Amsterdam, Netherlands.

SUDDEN DEATH OF A BOY OF 12 YEARS. J. P. L. HULST, Nederl. tijdschr. v. geneesk. **82**:3838 (Aug. 6) 1938.

Immediately after a romp with other boys an apparently healthy boy of 12 years died suddenly. The autopsy showed a highly dilated and hypertrophied heart; the microscopic examination demonstrated, in addition, chronic pancarditis, which might have been caused by an attack of influenza at the age of 3 years.

VAN CREVELD, Amsterdam, Netherlands.

FURTHER RESEARCH AND OBSERVATIONS ON FAMILIAL DEVIATIONS OF THE NUCLEI OF LEUKOCYTES (PELGER-HUËT). S. J. LEITNER and P. C. GUGELOT, Nederl. tijdschr. v. geneesk. **82**:3953 (Aug. 13) 1938.

Leitner and Gugelot studied three families in which 17 members showed the familial nuclear anomaly of the leukocytes described for the first time by Pelger in 1930 and by Huët in 1932. No sex difference in the incidence could be observed. There was no definite relation to tuberculosis. The investigation of the bone marrow showed that there was an abnormality in the formation of the cells. All three types of leukocytes showed the abnormality. After intracutaneous injections of tuberculin there was an increasing shift to the left in the leukocytic picture. In the peripheral blood there was no difference in phagocytosis from normal leukocytes of control persons. The immature cells of the bone marrow in the Pelger-Huët condition show, however, decreased phagocytosis; this may cause a decrease in the resistance of the organism. The familial nuclear anomaly of Pelger and Huët is the first known hereditary anomaly of the leukocytes.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

RETROPHARYNGEAL ABSCESS. C. W. EVATT, J. South Carolina M. A. **34**:287 (Nov.) 1938.

Retropharyngeal abscess may be acute or chronic. The chronic abscess is a tuberculous condition and usually is associated with Pott's disease or tuberculosis of the cervical glands. It is not discussed in this paper. Acute retropharyngeal abscess is usually caused by Streptococcus. At Roper Hospital in Charleston, S. C., the author reviewed cases of this disease in 4 adults and 8 children (3 under 1 year of age). The cases were distributed equally as to sex. The onset may be slow or rapid and is associated with tonsillitis. The condition should be diagnosed early and treated immediately with incision. It is best to have a tracheotomy outfit ready for use if necessary.

WESTON, Columbia, S. C.

SYMPOSIUM. WHAT IS JUSTIFIABLE TO DO IN OTITIC MENINGITIS: A BRIEF (HISTORICAL) REVIEW OF THE OPERATIVE TREATMENT OF PURULENT MENINGITIS. T. J. HARRIS, Laryngoscope **48**:458 (July) 1938. SURGICAL INDICATIONS IN SUPPURATIVE MENINGITIS. J. G. DWYER, ibid. **48**:461 (July) 1938. THE SURGICAL TREATMENT OF MENINGITIS. I. FRIESNER and H. ROSENWASSER, ibid. **48**:427 (July) 1938. SULFANILAMIDE AND RELATED COMPOUNDS IN THE TREATMENT OF MENINGITIS SECONDARY TO EAR AND SINUS INFECTIONS. E. APPELBAUM, ibid. **48**:482 (July) 1938.

Harris describes the methods and procedures offered since 1873 for the surgical treatment of purulent meningitis of otitic origin.

Dwyer emphasizes the need for a proper diagnosis of meningitis, made essentially from an examination of the spinal fluid. He deals extensively with the interpretation of findings in the spinal fluid to determine exactly the type of meningitis, if any, that is present. He states that the surgical treatment of meningitis is that of the focus of infection. He recalls that a cloudy spinal fluid may represent a tissue reaction to any irritant, including an infection. With no organism, the focus is still external to the meninges, and its surgical removal is strongly indicated. In the bacteriologic examination, it is suggested, a culture will be made more certain by planting 1 to 2 cc. of the centrifuged specimen.

Appended to the paper is a chart of the main points in the diagnosis of meningitis from the cerebrospinal fluid, as well as the questionnaire on a case of meningitis used by the New York Committee of the American Otological Society, Inc.

Friesner and Rosenwasser feel that the classification of meningitis into various forms according to the results of cytologic, chemical and bacteriologic examina-

tion is misleading and that the infection occurs in the tissues that comprise the meninges and not in the fluid itself. They say the changes in the fluid are merely expressions of the degree, severity, type and extent of the inflammation of the meninges and feel that the value of drainage of the fluid is theoretic. In discussing the surgical therapy they recommend:

1. For meningitis secondary to infection of the labyrinth, prompt labyrinthectomy with inspection of the dura of the middle and the posterior fossa, because the tendency for the infection to remain localized and heal is exceedingly slight.

2. For meningitis secondary to infection in the lateral sinus, an effort to get well beyond the limits of the disease, proximally and distally, laying the sinus open widely; if the bulb is thrombosed and purulent thrombi are present, drainage from the bulb by irrigation with diluted solution of sodium hypochlorite.

3. For meningitis secondary to infection in the middle ear, the mastoid and the petrous bone, after a complete mastoidectomy, a careful systematic search for leads into the petrous pyramid, the peribulbar cells and the zygoma by means of the Eagleton type of exploration until every pathway of extension has been carefully investigated, without opening the dura.

They conclude that the surgical treatment of meningitis is the early and adequate drainage of the focus from which the meningitis takes its origin.

In relating his experiences in using sulfanilamide in the treatment of otitic meningitis, Appelbaum states that smaller doses at more frequent intervals are more effective than larger doses at longer intervals, that the routine administration of sodium bicarbonate is advisable and that daily blood counts are important. In his series of 32 cases of pneumococcic meningitis 4 patients recovered. In the series of 26 cases of meningitis due to hemolytic streptococci 21 patients recovered and 5 died. He emphasizes the necessity of eradication of the primary focus and considers important the adequate drainage of the subarachnoid space by lumbar punctures (cisternal or ventricular if block occurs). He discourages radical methods of drainage, such as forced spinal or perivascular drainage.

In the discussion Eagleton recommended that after obliterating the primary focus of infection one open the cerebrospinal fluid system of the area where the infection entered, drain the infected fluid adjacent to the focus and then immediately close the dural opening with a piece of actively proliferating tissue, preferably mucous membrane of the lip or fascia lata. He feels that the cerebrospinal fluid adjacent to the focus of infection contains organisms in many cases in which the fluid drawn by lumbar puncture simply shows a high cell count.

Dr. Josephine B. Neal cautioned that cisternal puncture in cases of meningitis offers a different problem from cisternal puncture in cases of syphilis of the central nervous system because of the adhesions and congested blood vessels. She had heard of 25 or 30 fatalities in cases of meningitis, at the hands of experienced operators.

WOOD, Newark, N. J. [ARCH. OTOLARYNG.]

INTRACRANIAL COMPLICATIONS OF EAR DISEASE. J. P. STEWART, Practitioner **141**:603 (Nov.) 1938.

Suppuration occurring in the middle ear cleft may give rise to crippling disabilities, such as severe deafness, but it is only when suppuration extends beyond these boundaries that there is danger to life. The intracranial complications which follow acute and chronic suppuration are considered jointly, but there are certain distinctions. In acute infections the complications tend to be diffuse, and in chronic cases more circumscribed, in their initial stages. Thus in chronic cases initial circumscribed meningitis and delayed generalized meningitis and sinus thrombosis occur. Better results from treatment in the chronic cases might therefore be expected, and this is so.

This excellent article should be read in full.

GELSTON, San Francisco.

THE DEAF CHILD. P. FRANKLIN, Practitioner **141**:615 (Nov.) 1938.

A most interesting part of this article is that relating to mechanical aids to teaching the deaf.

Noises and speech sounds are communicated to the child by two types of electrical amplifiers: (1) electroacoustic; (2) electrovibratory. The electroacoustic apparatus is used to apply stimulation to the natural auditory channel. It is designed to produce sound through a microphone, either from the human voice or from gramophone records. Ear phones are applied to the ears. The electrovibratory apparatus is used to transmit vibrations to the finger tips. These rest on a delicately vibrating metal plate or vibrating cork. By analogy the finger tip serves as the ear, the vibrating plate or cork as the ear phones.

The children are divided into two groups: (1) those who have some remnant of auditory perception; (2) those who have no auditory perception and are therefore trained to receive the impression of sound or human speech through a substitute sense—touch, or the vibrotactile sense. In either group the child is encouraged to watch the teacher of speech form words. His attention is drawn to the appropriate toy, picture or letter spoken. In this way education is assisted as it would be in a normal child.

With reference to the sensory mechanism for feeling vibration, several writers have suggested an analogy between touch and hearing. Touch has been described as primitive hearing which in the course of evolution has been taken over by a specialized organ—the ear—for appreciating vibrations of a limited range—the human range of hearing. Experience with the speech training of deaf-mute children by touch supports the idea of a fundamental relation between the two senses. The use of touch is not new. For centuries deaf-mute children have been placing their fingers on the teacher's larynx to feel the vibrations of vocal sounds.

Emphasis is placed on preschool training, which at first is carried out individually and later in small groups.

GELSTON, San Francisco.

CONGENITAL LARYNGEAL STRIDOR. D. N. NICHOLSON, Tr. Med.-Chir. Soc. Edinburgh, 1938, p. 191; in Edinburgh M. J., October 1938.

Nicholson presented an infant of 6 months with this usually harmless type of noisy inspiration which alarms the parent. The stridor is at its maximum at about the sixth month of life, having become louder as the child got stronger. It slowly wanes, to disappear by the end of the second year. The child is not disturbed by the stridulous condition. Congenital webbing and papilloma must be ruled out in the diagnosis.

NEFF, Kansas City, Mo.

LARYNGEAL STENOSIS. C. E. SCOTT, Tr. Med.-Chir. Soc. Edinburgh, 1938, p. 192; in Edinburgh M. J., October 1938.

Two young children had undergone tracheotomy for nondiphtheritic stenosis. There were subsequent difficulties in closing the wounds and removing the tubes. Scott discusses the treatment of partial stenosis by the use of dilators and tubes.

NEFF, Kansas City, Mo.

TUBERCULOUS OTITIS MEDIA. R. B. LUMSDEN, Tr. Med.-Chir. Soc. Edinburgh, 1938, p. 193; in Edinburgh M. J., October 1938.

The clinician presented a boy who had entirely recovered from an extensive radical mastoid operation for tuberculous disease of the middle ear and gave the opinion that such otitis media is not rare, as he had seen several cases of it. When a young child suffers from an aural discharge that is resistant to treatment, tuberculosis should be thought of, and on repeated examination of the discharge tubercle bacilli may be found.

NEFF, Kansas City, Mo.

CLINICAL, ANATOMOPATHOLOGIC AND BACTERIOLOGIC STUDY OF TWO CASES OF ACUTE STENOSING LARYNGOTRACHEOBRONCHITIS, CHEVALIER JACKSON TYPE. P. ROHMER and C. OBERLING, Bull. Soc. de pédiat. de Paris **36**:242 (April) 1938.

Two girls, 6 years and 11 months old, respectively, died of acute suffocative tracheobronchitis. Necropsy confirmed the diagnosis. Abundant mucofibrinopurulent exudate completely obstructed the air passages in many places. In the older child the trachea and bronchi showed the most involvement, while in the younger one the small and medium-sized bronchioles were affected, and there were a few scattered areas of bronchopneumonia. In the latter case cultures made from the interior of the lung gave growths of Staphylococcus albus, Streptococcus haemolyticus, Fridländer's bacillus and a gram-negative bacillus of the colon group which did not ferment maltose. Experiments with the strain of Friedländer's bacillus which was isolated showed it to be very virulent for mice.

BENJAMIN, Montreal, Canada.

ROENTGEN TREATMENT OF THE TONSILS. BENASSI and M. SCARZELLA, Rev. franç. de pédiat. **14**:170, 1938.

Twenty-six cases are reported in which patients with diseased tonsils were given roentgen treatment in preference to tonsillectomy. In all the tonsils became smaller and more normal in appearance, and the clinical improvement in the general condition compared favorably with that obtained following tonsillectomy. The authors emphasize that roentgen treatment acts primarily on the infected, hypertrophied tissue and does not destroy the normal lymphatic tissue. They also state that the radiation stimulates the histiocytic response and so mobilizes forces combating infection. The details of the roentgen technic are given.

LESLIE, Evanston, Ill.

Diseases of Lungs, Pleura and Mediastinum

TWO CASES OF TOTAL PNEUMONECTOMY FOR BRONCHIECTASIS. R. M. WALKER, Proc. Roy. Soc. Med. **31**:1120 (July) 1938.

1. A boy of 9 years was shown before the section Nov. 22, 1935. In September he underwent left total pneumonectomy for bronchiectasis, which had been giving rise to symptoms since the first year of life.

2. A boy of 8 years, one of twins, at the age of 1½ years had an attack of bronchopneumonia which left him with persistent cough and sputum. In July 1937 he was admitted to the hospital. A full report is made of his condition on examination, of the operation performed and of the child's present condition.

WILLIAMSON, New Orleans.

EMPYEMA DUE TO STAPHYLOCOCCUS AUREUS IN AN INFANT 2 MONTHS OLD; TREATMENT WITH STAPHYLOCOCCUS ANATOXIN; CURE. AUZÉPY and MASCHAS, Bull. Soc. de pédiat. de Paris **36**:68 (Jan.) 1938.

Left-sided thoracic empyema developed in a girl 2 months old. Pus withdrawn from the chest revealed staphylococcus aureus. Numerous aspirations were performed. After the infant received injections of staphylococcus anatoxin she began to improve and recovered.

BENJAMIN, Montreal, Canada.

MULTILOCUATED ABSCESS OF THE LUNG IN AN INFANT, CURED BY TREATMENT WITH INTRAVENOUS INJECTIONS OF ALCOHOL. A. CAYLA, J. DELON and CORCELLE, Bull. Soc. de pédiat. de Paris **36**:92 (Feb.) 1938.

A 4 month old boy had what appeared to be two abscesses in the lower lobe of the right lung, complicating bilateral bronchopneumonia. The illness ran a

protracted course, and there was considerable mucopurulent expectoration. He was given an injection of 1 cc. of 30 per cent alcohol into the longitudinal sinus daily for twenty-five days and subsequently more intravenous injections of alcohol. Clubbing of the fingers developed, and the skin became hairy. These signs disappeared as he recovered. When seen at 16 months of age he seemed well, but it was believed that some bronchiectasis was present.

BENJAMIN, Montreal, Canada.

PURULENT MENINGITIS CURED BY SULFANILAMIDE; DISCUSSION ON THE NATURE AND POSSIBLE RELAPSE OF STREPTOCOCCIC MENINGITIS. R. MARTIN and A. DELAUNAY, Bull. Soc. de pédiat. de Paris **36**:107 (Feb.) 1938.

A boy 8½ years old had streptococcic meningitis, from which he recovered after treatment with sulfanilamide, given orally. Seven months after the onset of this disease purulent meningitis developed a second time, associated with rhinopharyngitis. No bacteria were demonstrated in smears or cultures of the spinal fluid during this recurrence of meningitis, but it is believed that the infection which was shown to be responsible the first time remained latent and later flared up, causing a recurrence of meningitis. He was again given sulfanilamide by mouth and again recovered.

BENJAMIN, Montreal, Canada.

MARCONI THERAPY IN NONTUBERCULOUS PULMONARY DISEASES. BENASSI and SCARZELLA, Rev. franç. de pédiat. **14**:188, 1938.

The treatment of 22 patients for thirty to forty minutes daily with 6 meter marconi waves led the authors to conclude that this method of treatment is of distinct value for pneumonia with delayed resolution and for pleuropneumonia and as an adjunct to thoracotomy in cases of purulent pleurisy. It is a method of promise also for pulmonary abscess.

LESLIE, Evanston, Ill.

PSEUDOMILIARY LESIONS IN THE LUNGS. L. C. ROJAS and A. GUZMAN, Rev. chilena de pediat. **9**:454 (Aug.) 1937.

Rojas and Guzman give the name "pseudomiliary lesions" to findings in roentgenograms of the lungs which are very similar to the findings in miliary tuberculosis. The diseases that particularly give such findings are pertussis, measles and influenza. The pathologic changes are due to peribronchitis and endobronchitis.

SCHLUTZ, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

OBSERVATIONS ON THE BLOOD SUGAR LEVEL BEFORE, DURING, AND AFTER HUNGER PERIODS IN HUMANS. W. W. SCOTT, C. C. SCOTT and A. B. LUCKHARDT, Am. J. Physiol. **123**:243 (July) 1938.

Determinations of blood sugar were made at ten minute intervals on 6 normal persons during the normal postabsorptive period and subsequently during hunger contractions. It was shown that with few exceptions the blood sugar ranged between 85 and 95 mg. per hundred cubic centimeters, indicating that the blood sugar curve during this period is a straight line and is unaltered by states of quiescence or of motility of the stomach.

NOURSE, Cleveland.

EFFECT OF ALCOHOL ON THE HUNGER SENSE. C. C. SCOTT, W. W. SCOTT and A. B. LUCKHARDT, Am. J. Physiol. **123**:248 (July) 1938.

A method of recording the intensity of hunger sensations was developed which made it possible to study the action of alcohol in relation to hunger. It was

found that the hunger contractions which occurred after the primary inhibition due to ingested alcohol produced hunger sensations which were more intense, even slight hunger contractions producing hunger pangs compared with the inconsequential effect of similar contractions occurring in a control period. Alcohol did not increase the amplitude of hunger contractions. In addition, alcohol produced an epigastric sensation during the period of alcohol inhibition preceding the hunger contractions. This feeling was associated with an increased desire for food but was less intense than hunger and continuous; consequently, it was considered to be appetite.

NOURSE, Cleveland.

DIAPHRAGMATIC HERNIA. A. BERNIER and A. GUILBEAULT, Union méd. du Canada **67**:125 (Feb.) 1938.

A newborn boy presented progressive cyanosis. The left side of the thorax was hyperresonant and immobile and produced no respiratory sounds. There was subcostal retraction. The heart was displaced to the right. The abdomen was retracted.

Autopsy showed a defect in the left side of the diaphragm, measuring 4 by 1.5 cm. Except the liver, the kidneys and the adrenal glands, all the abdominal organs and the descending colon were in the left side of the chest. The left phrenic nerve was present.

The authors discuss the various types of diaphragmatic herniation from an embryologic standpoint.

DAFFINEE, Boston.

PATHOLOGICAL REPORTS FROM THE CHILDREN'S HOSPITAL, MELBOURNE: I. PEPTIC ULCER IN INFANCY. R. WEBSTER, M. J. Australia **1**:1061 (June 18) 1938.

Chronic peptic ulcer was observed in a boy 4 months of age. The case history is of great interest in that the infant progressed well during the first month of life on breast feeding alone. When artificial feedings were started at the age of 1 month, he began to vomit and continued to vomit until death. The vomiting was not related to feedings, but it occurred several times a day and was occasionally projectile. The infant seemed to have attacks of severe pain at times and was ravenously hungry. He suffered from malnutrition, and pyloric stenosis was suspected, but the classic signs were absent. He died of bronchopneumonia, and postmortem examination showed a small ulcer on the posterior wall of the stomach immediately adjacent to the gastroduodenal junction. The ulcer showed such signs of chronicity as sharp definition, rolled over edges which were raised and indurated and a thickened base of circular shape, measuring 1.2 cm. in diameter. The loss of tissue involved the mucosa and submucosa. Since the usual causes of peptic ulcer are not operative at this early age, the question of etiologic factors is discussed.

GONCE, Madison, Wis.

PROBABLE DUODENAL ULCER IN A CHILD. L. BABONNEIX and ALDOU, Gaz. d. hôp. **111**:1207 (Sept. 21) 1938.

A 14 year old boy experienced an illness characterized by sudden onset of fever and headache. Epistaxis, hematemesis and bloody stools occurred on the third day of the illness. In the next six days three more hemorrhages occurred in the gastrointestinal tract, and once bleeding from the tonsils was observed. Hematologic studies gave negative results. A roentgenogram suggested duodenal ulcer. The patient recovered from the attack in a fortnight.

KAJDI, Baltimore.

RECTOSIGMOIDOSCOPIC EXAMINATIONS IN CHILDREN'S CLINICS. V. SANTAMARINA, Bol. Soc. cubana de pediat. **10**:349 (June) 1938.

Santamarina calls attention to the fact that rectosigmoidoscopic examinations should be done more frequently in cases of these conditions: difficulty in evacuation,

persistent constipation, passage of blood without apparent cause, rectal prolapse and pain in the anal region. He describes the work that has been done and the cases he has observed. The use of pentobarbital sodium as a sedative is recommended. An electrosigmoidoscope is used.

SCHLUTZ, Chicago.

CONGENITAL MEGACOLON IN A CHILD WITH MONGOLISM. B. CASTILLO, Bol. Soc. cubana de pediat. **10**:487 (Sept.) 1938.

Castillo describes a case of congenital megacolon in a mongoloid child 1 month old. Studies were made, but no evidences of obstruction were seen. The neurogenic factor is considered strongly, and a response to pancreatic extracts given by injection is claimed. Attention is called to the rarity of the occurrence of congenital megacolon in this type of patient.

SCHLUTZ, Chicago.

RECURRENT APPENDICITIS. L. DRÜNER, Beitr. z. klin. Chir. **164**:394, 1936.

Because the normal appendix is sensitive to pain and because it is known that during infection of this organ there is injury to the nerves so that receptability is reduced, recurring attacks of appendicitis are not as acute and painful as the first attack. This should be taken into account.

RUBIN, Boston.

CORRELATION OF CECUM AND LIVER IN CLINICAL CONDITIONS IN CHILDREN. V. MIKULOWSKI, Jahrb. f. Kinderh. **147**:29 (June) 1936.

Two cases in which purulent hepatitis occurred in the course of recurrent appendicitis are reported. In both the illness ended fatally. The diagnostic difficulties are stressed. The frequency of the association of inflammatory lesions of the appendix with lesions of the liver and gallbladder is stressed. The literature is reviewed.

LANDAU, Hannibal, Mo.

ICTERUS GRAVIS WITH ECLAMPSIA IN A CHILD DURING THE FIRST YEAR OF LIFE. E. LOHSE, Jahrb. f. Kinderh. **147**:40 (June) 1936.

An 11½ month old boy had had occasional convulsions since birth. He had had no digestive disturbances. The Wassermann test was negative on two occasions. He was admitted to the hospital because of vomiting and loose stools. Later, jaundice developed; this was followed by convulsions and death. High grade fatty and parenchymatous degeneration of the liver was found at autopsy.

The theory of chronic disease of the liver is advanced (sustained by pathologic examination). It is felt that the illness was a result of chronic liver insufficiency and the inability of the liver to remove toxic substances, the free circulation of which gave rise to the cerebral symptoms which preceded death.

LANDAU, Hannibal, Mo.

NAVEL COLIC. A. PEIPER and E. HOFMANN, Monatschr. f. Kinderh. **75**:306 (Sept.) 1938.

For years the syndrome of recurring attacks of pain around the navel has been ascribed to innumerable causes. It is usually considered a neurosis. The writers report 4 cases in which roentgenograms showed changes of the type due to gastric and duodenal ulcer.

GERSTLEY, Chicago.

CONGENITAL PYLORIC STENOSIS AND THE RESULTS OF TREATMENT. MARIE MASKOVA, Časop. lék. česk. **75**:931 (July 17) 1936.

A short review of the literature is followed by a résumé of the observations in 26 cases. The patients included 21 boys. Only 4 patients were premature infants. No hereditary tendency was noted. Among other symptoms were hypo-

chloremia and increased bicarbonate content in the blood. Spasmophilia does not appear in spite of the alkalosis. Both peristaltic waves and a palpable tumor were found in 19 infants, peristaltic waves alone in 2, tumor alone in 4, and in only 1 infant were neither waves nor tumor found. All but 1 patient were operated on, and 6 of those operated on died. Of these, 2 were in an extreme state of malnutrition, 1 had persistent postoperative bleeding from the wound, 1 vomited from the third day of life and continued to vomit profusely after operation, 1 had severe asthenia following pyodermia and at autopsy had purulent peritonitis, and 1 was in very poor condition, weighing 2,950 Gm. at the age of 2 months. The operation of choice was the Hildebrandt modification of the Rammstedt operation, which consists in dull dissection of the terminal tumor fibers. STULIK, Chicago.

Nervous Diseases

OTITIC MENINGITIS DUE TO STREPTOCOCCUS HEMOLYTICUS: OPERATION AND RECOVERY. M. H. KAIDEN, New York State J. Med. **38**:1026 (July 15) 1938.

Streptococcic meningitis from otitis media is reported in a boy aged 7 years. By the time the meningitis developed, the ear was apparently normal. However, it was thought advisable to do a mastoidectomy. No pus, softening of bone or congestion was found. The case cleared up after administration of sulfanilamide and prontosil soluble (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate, now known as neoprontosil).

AIKMAN, Rochester, N. Y.

SPASTIC CONDITIONS IN CHILDREN. C. S. LARGE, Irish J. M. Sc., November 1938, p. 727.

This article written by an orthopedist to physicians and to staffs of hospitals for obstetric patients is a plea for better care on the part of attendants at childbirth. In Large's small series the largest number of the spastic conditions were seen in children who had been delivered in hospitals. In homeborn children the distribution was equal for those delivered by midwives and those by physicians. He says that there are three main causes: prenatal, natal and postnatal conditions. He assumes that in the majority of cases the spastic condition arises as a result of damage incurred during the natal period. No evidence is submitted in the report to show whether any investigation, such as the study of an encephalogram, had been carried out to determine the source of the spastic condition. It appears to be a rather broad assumption to take for granted that injuries incurred during delivery are the whole cause of the trouble. SNELLING, Toronto, Canada.

PSEUDOHERMAPHRODITISM, ADIPOSITY, POLYURIA AND HYPERGLYCAEMIA: AN INFUNDIBULO-TUBERIAN SYNDROME. R. M. STEWART, J. Neurol. & Psychiat. **1**:68 (April) 1938.

Stewart reports the case of a boy aged 17 years who was normal at birth except for external pseudohermaphroditism and who acquired in his third year marked obesity and retardation of growth and intelligence, with typical features of adiposogenital dystrophy. Later, polyuria, polydipsia, excessive somnolence and hyperglycemia developed. There were severe chronic degenerative changes in the hypothalamic nuclei, especially in the nucleus supraopticus, nucleus tuberis lateralis, nucleus tuberomamillaris, nucleus paraventricularis and the substantia grisea of the third ventricle. The cellular loss was most marked in the tuberal and paraventricular nuclei and was less evident in the nucleus tuberomamillaris. The nerve cells of the nucleus supraopticus were less altered, but both here and in the nucleus paraventricularis there was intense gliosis. According to Stewart, the clinical

picture was conditioned not by alterations limited to the pituitary gland but by disturbance of the reciprocal interactions between the pituitary and the hypothalamic nuclei which regulate its activities. Because of the diffuseness of the lesions, it was difficult to determine the more exact location of the structures responsible for the individual symptoms.

MALAMUD, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT OF PURULENT STREPTOCOCCIC MENINGITIS BY SULFANILAMIDE. R. MARTIN and A. DELAUNAY, Ann. méd.-chir. **3**:86 (March) 1938.

Purulent meningitis caused by organisms of the streptococcus group is relatively rare and the cases constitute only about 6 per cent of all cases of meningitis. In most of the cases the disease is secondary to infectious processes in the ears or nose. The mortality varies from 97 to 100 per cent. Recently, the use of sulfanilamide has been followed by recovery in cases of meningitis of this type. Large doses, up to 0.5 Gm. every two hours, have been given, followed by gradual diminution of the dose to 4 and then to 3 Gm. daily. In infants a dose of 0.001 Gm. per kilogram of body weight has been used. In certain cases intraspinal administration is advisable; the authors advocate the use to from 10 to 20 cc. of an 0.8 per cent solution daily, accompanied by drainage of the cerebrospinal fluid. In all cases in which the meningitis is secondary to a localized infectious process, there should also be surgical intervention.

DE JONG, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

SEROUS APOPLEXY IN CHILDREN IN THE COURSE OF TREATMENT WITH ARSENOBENZENES. LINOSSIER-ARDOIN and RONGET, Bull. Soc. de pédiat. de Paris **36**: 286 (April) 1938.

Four children had reactions of a rare type following injections of arsenical preparations, although they had received many similar injections previously without any untoward effects. Each of these reactions, which are characterized as serous apoplexy, occurred a few days after an injection and consisted of headache, occasionally accompanied by nausea, followed by epileptiform convulsions and coma. The spinal fluid, examined in only a single case, showed an increase of protein but no pleocytosis and was not under abnormal pressure. Two of the children died. The two who recovered showed no abnormal sequelae. A warning is sounded against indiscriminate injection of arsenical preparations for conditions other than syphilis.

BENJAMIN, Montreal, Canada.

TWO CASES OF SEROUS APOPLEXY IN CHILDREN. J. CATHALA, P. AUZÉPY and A. BRAULT, Bull. Soc. de pédiat. de Paris **36**:291 (April) 1938.

A boy 9½ years old had a severe reaction four days after an injection of an arsenical preparation. He showed coma, convulsions, signs of meningeal irritation and fever. The margins of the optic disks were slightly blurred. A second boy, 3 years old, had a similar reaction forty-eight hours after an injection of sulfarsphenamine. Each child had received similar injections previously without such alarming sequelae. The spinal fluid of both boys showed increased protein, and that of the second was slightly xanthochromic. Both recovered.

BENJAMIN, Montreal, Canada.

CONGENITAL, HEREDOFAMILIAL DISEASE, CONSISTING OF RHYTHMIC TREMOR OF THE HEAD, EYES AND UPPER EXTREMITIES. L. VAN BOGAERT and E. DE SAVITSCH, Encéphale **1**:113, 1937.

Van Bogaert and de Savitsch report on a congenital syndrome characterized by rhythmic horizontal oscillations of the eyeballs, with occasional elevation and circumduction and synchronous palpebral movements; rhythmic oscillations of the

head and arms, increased by movement and emotion; dystonic anteflexion of the neck; absence of automatic associated movements of the arms; relative immobility of the trunk; epilepsy, and, occasionally, feeblemindedness or varied psychotic disturbances. The tremors of the eyes and upper extremities were the most constant feature. In a family of 109 descendants 40 were afflicted. Three generations were studied. This disease is believed to be distinct from essential hereditary tremor, hereditary nystagmus, paramyoclonus multiplex, Morvan's chorea, electric chorea, tic and myoclonus epilepsy. It corresponds to the hereditary "nystagmus-myoclonia" described by Lenoble and Aubineau (*Rev. de méd.*, vol. 25, Oct. 1, 1905; ibid. **31**:208, 1911). This condition occurs in about half the offspring of affected persons. The sexes are equally involved. Dominance is not complete, as the condition may remain latent until revealed in the offspring of two phenotypically normal persons descended from affected stock. There is no correlation with multiparity or with the order of birth.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

SYNDROME CHARACTERIZED BY PROGRESSIVE CEREBELLAR ATAXIA WITH FEEBLEMINDEDNESS. M. MAERE and G. MUYLE, J. belge de neurol. et de psychiat. **38**:96 (Feb.)) 1938.

Maere and Muyle report the cases of 2 young Polish Jews, a brother and a sister, who presented early in life a syndrome consisting of progressive ataxia, skeletal anomalies and arrested mental development. They showed generalized hypotonia, dysmetria, asynergy and dysdiadokokinesia, with difficulty in walking. Both showed nystagmus and incoordination of ocular movements. The brother had certain skeletal changes—scoliosis, brachydactyly and reduction in the size of the cranium—and the sister showed precocious sexual development. No other members of the family had similar difficulties. The authors compare the findings with those observed in Friedreich's ataxia. They believe that the two conditions are different.

DE JONG, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

A CASE OF HEPATOLENTICULAR DEGENERATION FOLLOWING TRAUMA. R. SCHWARZ and R. LEDERER OVA, Rev. neurol. **69**:410 (April) 1938.

A boy of 12 fell from his bicycle, fracturing his left clavicle. The left arm became progressively weaker. Ten months later speech difficulty and mental changes developed. Dysarthria, dysphagia and hypersalivation were present. There were an intention tremor and a typical corneal ring. The tendon reflexes of the legs were normal.

DAFFINEE, Boston.

"NEURO-UVEO-PAROTITIS." G. DE MORSIER and R. FRANCESCHETTI, Rev. neurol. **69**:688 (June) 1938.

A case of Heerfordt's syndrome is described with involvement of the hypothalamus. A 12 year old boy, underdeveloped sexually, presented polydipsia and polyuria. At the age of 15 he began to lose weight rapidly and slept a great deal, and serous iridocyclitis developed. Hard, nontender swelling of both parotid glands was present. Fluid from the anterior chamber of the eye was injected into a guinea pig, but no lesions of tuberculosis appeared.

DAFFINEE, Boston.

STUDY AND TEATMENT OF HEREDOFAMILIAL DISEASES WITH PREDOMINANT LESIONS IN THE SPINAL CORD. R. SOTO ROMAY, Semana méd. **45**:897 (April 28) 1938.

Soto Romay states that the various heredofamilial diseases with predominant lesions in the spinal cord are clinical forms of a process of degeneration of certain

segments of the nervous system. The group of familial diseases with lesions in the spinal cord have many common symptoms and analogous anatomicopathologic lesions. There are atypical types and transitional forms between familial spasmodic paraplegia, progressive amyotrophy of the Charcot-Marie type and Friedreich's hereditary ataxia. In the course of the disease the patient may show transformation of one type to another or association of two or more atypical forms of the disease. The author reports 3 cases. The patients were a mother and her 2 children. The 3 patients suffered from a combined form of spasmodic paraplegia, progressive amyotrophy and hereditary ataxia. In all 3 patients the factors of heredity and infection existed. Amyotrophy of the distal part of the legs as well as of the feet and hands was severe in the mother and in the oldest son, aged 13 years. The disease was of slow evolution in the mother, acute in the son and latent in the daughter, aged 7 years. Microscopic study of the amyotrophic muscle, a specimen of which was taken for biopsy, showed waxy degeneration of the muscular fibers, with loss of striation. There were proliferation of the sarcolemmal nuclei, perivascular infiltration and proliferation of the interstitial tissue. The author reports satisfactory results of combined treatment with vitamins and liver extracts. The evolution of the disease stopped, and the patients gained some muscular force and control of the nervous symptoms. The author calls attention to the diagnostic value and significance of the contralateral Schaeffer sign, which is positive in acute hereditary neurologic diseases and indicates involvement of the pyramidal segment. It was positive in the author's male patient.

[EDITOR'S ABSTRACT. ARCH. NEUROL. & PSYCHIAT.]

PROTECTIVE REFLEXES. A. PEIPER, Jahrb. f. Kinderh. **146**:233 (April) 1936.

In a study of protective skin reflexes it was found that in young infants localized irritation of the skin releases certain reflex movements. The localized movements are finally followed by movements of a more generalized nature and crying.

LANDAU, Hannibal, Mo.

FURTHER STUDIES ON THE PROBLEM OF CHOREA MINOR: CLINICAL ETIOLOGIC AND PATHOLOGIC ASPECTS. O. KRONIG, Jahrb. f. Kinderh. **146**:329 (May) 1936.

The usually acknowledged association of chorea and classic rheumatic fever is discussed. No specific agent has been demonstrated. The spread of the virus through the nervous system is thought to be by way of the spinal fluid and blood. Treatment is symptomatic and by sedation.

LANDAU, Hannibal, Mo.

DIAGNOSIS OF ENCEPHALITIS IN INFANCY. G. DE LANGE, Monatschr. f. Kinderh. **75**:264 (Sept.) 1938.

This is a lengthy discourse with the submission of several case reports as evidence that many illnesses diagnosed as encephalitis are in reality toxic encephalopathy.

GERSTLEY, Chicago.

HEREDITY IN EPILEPSY: IV. STUDY OF THE CHILDREN OF EPILEPTIC PATIENTS. K. CONRAD, Ztschr. f. d. ges. Neurol. u. Psychiat. **159**:521 (Sept.) 1937.

Conrad used the material collected during a census of defective persons in Wartenburg, Bavaria. This included cases of a condition classified as "repeated epileptic attacks." A thorough study of 519 patients was made. Most of the patients suffered from epilepsy of long standing and had children. The patients were divided into three main classes: those with idiopathic epilepsy, 55.3 per cent; those with an intermediate form, 24.2 per cent, and those with symptomatic epilepsy, 14.2 per cent.

The intermediate class (134 patients) needs comment. Patients with the following types of the disease were included in this group: late onset of epilepsy, between the ages of 30 and 50, 33 patients; first attack after an explosion, 14 patients; first attack after probable and definite commotio, 26 patients; neurosyphilis, 9 patients; severe alcoholism, 9 patients; suspected tumor of the brain, 3 patients; first attack after an infectious disease, such as malaria, 2 patients; typhus, 2 patients; otitis media, 1 patient, and meningitis, 2 patients. Conditions associated with deafness, blindness, hypertension, postpartum embolism, injury to the spinal column, carbon monoxide intoxication, lead poisoning, questionable tetany, early schizophrenia and diffuse sclerosis were included.

When the children who died in early infancy were excluded, an incidence of epilepsy of 6 per cent was found among the children of epileptic parents. The incidence was higher in the idiopathic group (from 6 to 8 per cent) than in the symptomatic group (from 1 to 2 per cent). Conrad believes that these figures indicate a genetic component even in the symptomatic form. The figures indicate a frequency four times as great as that in the population (0.3 per cent).

Mental deficiency was found in 16.5 per cent of the children of patients with idiopathic epilepsy, in 6.3 per cent of children of patients in the intermediate group and in 2.5 per cent of children of patients in the symptomatic group. The figure for the idiopathic group is high. Conrad cites as a control the normal group studied by Juda, who found from 5 to 6 per cent mentally defective children among the siblings, nephews and nieces of normal pupils.

Psychoses were found in 3.7 per cent of children of epileptic persons, as compared with an incidence of 1.2 per cent in the general population (excluding persons with dementia paralytica). The figure for the intermediate group was 0.9 per cent. There were no psychoses in the children of persons in the symptomatic group. Abnormal personalities were found in 8.4 per cent of the children of the idiopathic group, in 3.4 per cent of the children of the intermediate group and in 0.7 per cent of the children of the symptomatic group. So-called functional disorders (stuttering, enuresis, migraine, asthma, vasomotor instability and disturbances in sleep) were noted in the children of epileptic patients, with the following frequency: in the idiopathic group, 7.5 per cent; in the intermediate group, 4 per cent, and in the symptomatic group, 4.3 per cent. Morphologic disorders (clubfoot, congenital dislocation of the hip, oxycephaly, tuberous sclerosis, eczema and kyphoscoliosis) were found in 5.9 per cent of children of the idiopathic group, in 4.9 per cent of children of the intermediate group and in 1.4 per cent of children of the symptomatic group. Children of persons with idiopathic epilepsy are more abnormal than other children in every respect. If criminals are included, 42 per cent of the children of persons with idiopathic epilepsy have some type of physical or mental abnormality. Conrad believes that there is a constitutional factor even in symptomatic and exogenous forms. Persons who react to noxious agents with the convulsive state are predisposed in some way. There is no evidence of sex linkage in the transmission of epilepsy.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

GENETIC STUDIES OF CHILDREN OF EPILEPTIC PARENTS. G. FRANKE, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:381 (Nov.) 1937.

Franke reports a study of 106 institutionalized epileptic patients each of whom had at least 1 child 5 years of age. There were 187 children of 71 patients with idiopathic epilepsy and 97 children of 35 patients with symptomatic epilepsy. The percentage of epilepsy for the population used as a control, including only children over 10 years of age, was 0.3. With the same method of computation, the figures were 3.4 per cent for the children of persons with idiopathic epilepsy and 2.4 per cent for the children of persons with symptomatic epilepsy. If the offspring between 5 and 20 years of age were considered only as ½ unit and those over 20 as 1 unit, the figures were 3.9 per cent for the children of persons with idiopathic epilepsy and 2.6 per cent for the children of persons with symptomatic epilepsy.

If children up to 30 years of age were counted as ½ unit, the figures were 5.1 per cent and 3.1, respectively. The percentage of mental deficiency for the children in this series over 10 years of age who had epileptic parents was 12.2. The figures for the average population are from 1 to 2 per cent. It must, however, be noted that of 20 mentally defective children of parents with idiopathic epilepsy 15 had mentally defective parents; the remaining 5 defective children had parents of borderline intelligence. Of the mentally defective children of persons with symptomatic epilepsy 4 of 5 had defective parents.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

EPILEPSY AND ALIMENTARY HYPOGLYCEMIA. H. J. SCHOU, Acta psychiat. et neurol. **12**:533, 1937.

Many epileptic persons show alimentary hypoglycemia sufficiently low to cause convulsions. The alimentary hypoglycemia can be demonstrated in about 40 per cent of epileptic patients, provided blood sugar curves are obtained for four hours. Schou analyzed 100 nonselected cases of epilepsy in patients of both sexes who were over 15 years of age. Determinations of the blood sugar were made every fifteen minutes for the first hour and every thirty minutes for the following three hours, making ten determinations in all for each test. All curves which showed a fasting level below 60 mg. per hundred cubic centimeters, a maximum rise of less than 120 mg. or a fall to below 50 mg. after four hours were considered abnormal. Thirty patients showed a fasting level of the blood sugar below 60 mg. per hundred cubic centimeters; 34, a maximum rise to less than 120 mg., and 43, a level below 50 mg. after four hours. Thus, 43 per cent of the epileptic patients studied showed evidence of alimentary hypoglycemia. With 23 patients the sugar tolerance test was repeated two or three times, with intervals up to one year between tests; 15 patients who had low curves during the first test showed hypoglycemia in one or more subsequent tests. Thus, in most patients the alimentary hypoglycemia was a permanent phenomenon. The average age of the 43 patients who had normal sugar curves was 39, and the average duration of epilepsy in this group was twenty-one years. The average age of the 57 patients who had hypoglycemic curves was 33, and the average duration of the epilepsy in this group was seventeen years. Thus, alimentary hypoglycemia occurred mostly in young epileptic patients with a relatively short duration of epilepsy. In the case of 7 epileptic patients who were able to attend to their routine work and to take the usual diet, double determinations of the blood sugar were made every hour, from 7 a. m. to 10 p. m., making sixteen double determinations in all. It was found that the patients with sugar tolerance curves denoting hypoglycemia showed low sugar curves for the day. Thus, a case was noted in which the blood sugar level fell below 60 mg. per hundred cubic centimeters and remained at that level for several hours. In another the blood sugar level remained constantly below 60 mg. per hundred cubic centimeters throughout the day, in spite of meals and work. For 29 patients with low sugar curves, the average incidence of the fits per twenty-four hours was calculated for fifteen years and plotted on the curve in terms of percentages of fits for each hour of the twenty-four hour period. The curve showed two absolute peaks, one from 6 to 8 a. m. and one from 9 to 12 p. m., and two relative peaks, one from 11 a. m. to 1 p. m. and the other from 5 to 7 p. m. The absolute peak in the evening, coinciding with the first hours of sleep, appeared to be unrelated to the hypoglycemia, but the absolute morning peak and the relative noon and late afternoon peaks might be explained by the fact that it was during these periods of the day that the alimentary hypoglycemia usually occurred. The author emphasizes the importance of occult hypoglycemia as a factor inducing convulsions in many epileptic persons and discusses the treatment of convulsions so caused. The treatment may be surgical (partial resection of the pancreas) or medical. The latter consists in maintenance of the patient on a diet rich in carbohydrates and administration of from 50 to 100 mg. of ephedrine three times daily.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

FOUR CASES OF LEUKODYSTROPHIA CEREBRI HEREDITARIA PROGRESSIVA (MERZBACHER-PELIZAEUS' DISEASE. R. FORSBERG and R. STRØMME, Acta psychiat. et neurol. **12**:639, 1937.

The authors report clinically the cases of 1 brother and 3 sisters, aged 13, 7, 5 and 4 years, respectively, who showed progressive rigidity with contracture in flexion of the lower extremities, pes cavus, intention tremor, spontaneous nystagmus, ataxia, dysarthria and mental deterioration. For 2 of the patients there was roentgenographic evidence of osteomalacic changes in the bones of the feet. A sister aged 21 showed similar symptoms but milder, and 1 male cousin of the patients' grandparents was mentally deficient and dysarthric and had difficulty in walking. The authors classify the condition presented by their 4 patients as Pelizaeus-Merzbacher disease.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

ADAPTATION TO REALITY IN EARLY INFANCY. T. BENEDEK, Psychoanalyt. Quart. **7**:200, 1938.

Benedek points out that infants who have been raised in a hospital or who have suffered from lack of love or too rigid a routine differ in their adaptation to reality from infants whose routine has been adapted to their physiologic needs and whose mothers have loved them. In the second group, the infant's ego is assured, enhanced by a reliable ally, the mother, who regulates the things of the outer world and saves the child from anxiety. The ego, strengthened, on the one hand, by the libidinal relation to the mother and, on the other, by the absence of anxiety, has a greater capacity to perceive the objects of the outer world. This ego is able to accept new and unexpected situations and to master them by trust in the mother. In the adaptation to reality it has a greater span and a greater versatility. In the first group, the infant is deprived of its powerful ally, the mother, to whom the child capable of waiting can turn with the conviction that help and satisfaction will come from her. The infant who cannot entrust itself to the mother is left alone; it turns its attention libidinally not to the mother but to the objects surrounding it. It is abandoned by the mother as much as by the other objects of the world and therefore concentrates its weak ego on material things and tries to control them in an attempt to save itself from any new situation which is frightening. The infant becomes dependent on the sequence of the procedure of nursing, on the manipulations of the nursing persons and on the articles used. It cannot establish confidence as the primary object relationship, and a greater amount of anxiety develops. This anxiety has several sources. One is the body itself, which causes the infant pain by traumatic sensations of unsatisfied instinctual needs. Another source of anxiety is the real danger in which the weak ego finds itself in the object world. A third source, at a later age, is the instinctual tension which develops as a result of the disturbance of the object relationship to the mother.

Observation of children and the analysis of adults in recent years show an increasing number of rejected children and adults with the psychologic reactions of the rejected child. Benedek points out that this must result from the rigid routine laid down by pediatricians. Infants born in this hygienic age are raised by a strict ritual, which is dictated from the first moment of life by what seems to be the most important element in civilization, time. The child has to be adapted to the time regulations of the hospital or of the home. The technic of feeding as it is practiced directly contradicts all the leading principles of education. The endeavor in education is to find a way to satisfy the needs of the child which guarantees the best development of the personality; all modern studies of educa-

tion are aimed toward finding methods to save the child from feelings of inferiority and from the undermining of its ego.

Why is it that in this "century of children" mothers so readily accept the rigid type of hygiene as the highest precept in their relationship to their infants? Why do they relinquish so easily their emotional relation to the child and often "reject" it with the rationalization that they are doing only what is permitted and, therefore, what is best? It is probable that mothers tend at present to make their children adhere to schedules for the sake of the schedule, not for the sake of the child, for this is "the century of the woman." It is the emancipation of women that elevated nursery hygiene to its present height and, with the help of narcissistic satisfaction, intellectualized the mother's relationship to the child.

PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

A CRITICISM OF MENTAL TESTING. J. C. HILL, Brit. J. M. Psychol. **17**:258 (March) 1938.

In an infants' school in a poor area of London, 62 children 7 years of age were tested by the usual methods, and 8 (13 per cent) were found to be definitely backward. However, when they were interviewed individually and given compositions to write, it was difficult to say that any one of the children was stupid. A review of elemental material enabled many of them to take their places with average pupils. Hill criticizes the attitude that there is a definite entity called intelligence, the amount of which is fixed for every individual persons and can be measured at any time. A child who falls behind in reading soon falls behind in everything and obtains low results in tests. Some children cannot do ordinary sums merely because they do not know the tables or have had no experience in counting concrete things. Mental testers assume that all children in a class have had equal opportunity of acquiring everyday knowledge, and for convenience they disregard the environmental influences of the first five years, thereby ignoring important factors such as absences, changes of school, poor eyes, lack of sleep and emotional disturbances.

ALLEN, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

SCHIZOPHRENIA-LIKE PSYCHOSES IN YOUNG CHILDREN. R. A. Q. LAY, J. Ment. Sc. **84**:105 (Jan.) 1938.

Lay reports 6 schizophrenia-like psychoses in children between 3 and 5 years of age whose behavior seemed to place them in the group with dementia infantilis. In 4 of the patients the picture corresponded to that of dementia infantilis; in 1 the disease was obviously epidemic encephalitis, and in 1 there was a hyperkinetic syndrome. The prognosis is poor in all except the child with the hyperkinetic syndrome. Differentiation of the syndrome is difficult and treatment ineffective.

KASANIN, San Francisco. [ARCH. NEUROL. & PSYCHIAT.]

SCHIZOPHRENIFORM PYCHOSES IN CHILDHOOD. G. LANGFELDT, Encéphale **1**: 183, 1937.

In a group of 40 children hospitalized in a psychiatric service the condition of 4 was diagnosed as schizophrenia. The ages varied from 12½ to 15 years. Two were boys. Two were girls. One was an imbecile. One had presented hysteriform manifestations before the onset of schizophrenia, and 1 had always had a tendency to autism. Only 1 had hallucinations. The dominant clinical features were stereotypy, autism and anomalies of affectivity. Delusions of influence, of derealization and of depersonalization were not observed. There was no schizoid heredity. The main causes were believed to be psychogenic. The absence of depersonalization is explained by the incomplete development of the feeling of personality in children, as in mentally deficient persons.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

SOME HYSTERICAL SYNDROMES AT PUBERTY AND AT PREPUBERTAL PERIODS. E. MESSERI, Riv. di clin. pediat. **36**:591 (July) 1938.

Hysteria in 4 girls 11 to 15 years of age is reported. One patient had as her only symptom hyperthermia, with the body temperature at times as high as 42 C. (107.6 F.). Laryngospasm was the manifestation in another, while paralysis of the legs was present in the other 2. Fright was a definite etiologic factor in 2 of these patients.

HIGGINS, Boston.

MONGOLIAN IDIOCY. TOBLER, Monatschr. f. Kinderh. **76**:62 (Oct.) 1939.

Mongolian idiocy in twins is reported. That the twins were identical is shown by sex, color and pigmentation of the skin, color and structure of the iris, color, length and arrangement of the hair, shape of the cranium and face, appearance of ears, nose and mouth and blood grouping.

GERSTLEY, Chicago.

MENTAL DISTURBANCES IN CHILDREN RESEMBLING SCHIZOPHRENIA. T. RAMER, Acta psychiat. et neurol. **11**:489, 1936.

In a study of 417 children in a clinic for child guidance, Ramer found about 2 per cent with schizophrenoid syndromes. Mental disturbances of a schizophrenic type are more difficult to recognize in children than in adults. Many features of the child's behavior resemble the catatonic syndrome in adults, e. g., the tendency to rhythmic repetition in speech and movements, stereotypy, grimacing, mannerisms, negativism, suggestibility, intellectual-emotional dissociation and impulsive reactions. These traits of infantile behavior may be exaggerated to an abnormal degree and may become associated in time with graver symptoms of dissociation of personality and deterioration. Cases of schizophrenia in children of from 12 to 15 years have been reported by numerous writers. Ziehen traced the onset of symptoms to the seventh year in some cases of schizophrenia. The clinical picture observed in children more closely resembles that of schizophrenia of adults as the child nears puberty. In most instances the differential diagnosis lies between schizophrenia and various organic infantile dementias, such as the late form of amaurotic family idiocy and encephalitis.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Genitourinary Tract

DIRECT EVIDENCE OF FUNCTION IN KIDNEY OF AN EARLY HUMAN FETUS. G. CAMERON and R. CHAMBERS, Am. J. Physiol. **123**:482 (Aug.) 1938.

The tissue culture method was used to study the function of the kidney of a 3½ month fetus. The cut ends of the segments of the tubules healed over in the culture. Phenol red and orange G added to the medium passed into and accumulated in the lumens of the proximal tubules to a conspicuously higher concentration than that of the dyes in the medium. The experiments with phenol red showed that the fluid of the human metanephros had a p_H of approximately 7, while that of the culture medium was from 7.4 to 7.6.

These results constitute the first direct evidence that human embryonic proximal tubules of themselves are able, at least at 3½ months, to function.

NOURSE, Cleveland.

NEPHRITIS WITH ALBUMINURIC RETINITIS AND PATENT DUCTUS ARTERIOSUS. W. R. S. DOLL and J. WATTS, Proc. Roy. Soc. Med. **32**:95 (Dec.) 1938.

The patient was a girl aged 9 years. She was admitted to the hospital with the complaint of headaches and vomiting for three years and hematuria for eight

months. The family history, the past history and the results of the physical examination and of other investigations are given in the report.

WILLIAMSON, New Orleans.

COEXISTENCE OF AN ABNORMALITY OF THE VESICAL NECK AND BILATERAL MEGAURETER IN A CHILD EIGHT YEARS OLD; MULTIPLE OPERATIONS; FUNCTIONAL CURE. BOPPE and MARCEL, Bull. Soc. de pédiat. de Paris **36**:36 (Jan.) 1938.

An 8 year old boy had incontinence of urine. He had been subjected to circumcision and an operation for hypospadias. As the condition showed no improvement, he was readmitted to the hospital for investigation. On intravenous pyelographic and cystoscopic examination and ureteral catheterization it was found that both ureters were markedly dilated and tortuous and that there was muscular hypertrophy of the ureters for a short distance above the ureterovesical junctions. The urine contained pus and staphylococci. Meatotomy was ineffective, and bilateral nephrostomy was done. The wound drained for six months, and then resection of the hyperplastic portions of the ureters was done, with transplantation of the shortened ureters into the bladder. After a few months the boy voided through the urethra in a normal manner but still wetted the bed occasionally.

BENJAMIN, Montreal, Canada.

FAVORABLE ACTION OF SULFANILAMIDE (1162 F) ASSOCIATED WITH LOCAL TREATMENT IN GONOCOCCIC VULVOVAGINITIS IN LITTLE GIRLS. R. MARTIN and A. DELAUNAY, Bull. Soc. de pédiat. de Paris **36**:112 (Feb.) 1938.

Two girls, 6 and 7 years old, were treated for gonococcic vaginitis by local instillation of permanganate solution (1 in 4,000) and by oral administration of sulfanilamide. The first girl had acute vaginitis and was cured in eight days; the second was cured in fifteen days, after she had been treated successfully by various methods over a period of seven months. BENJAMIN, Montreal, Canada.

PASSAGE OF THE PIGMENT OF THE RED BEET INTO THE URINE OF A CHILD. HALLÉ and GIRARD, Bull. Soc. de pédiat. de Paris **36**:266 (April) 1938.

Reddish-colored urine from a boy after he had ingested beets contained no blood, albumin or hemoglobin. The color was due to a vegetable pigment closely resembling carotene. To explain why only one child of a number who partook equally of the same dish of cooked beets had pigmented urine, the hypothesis is offered that as the pigment is attached to the saccharides of the beet the renal threshold for these saccharides may be lower in the child in question as compared with the others. It is important, of course, not to mistake this pigment for blood in the urine.

BENJAMIN, Montreal, Canada.

TREATMENT OF GONOCOCCIC VAGINITIS IN INFANCY WITH SULFANILAMIDE. A. J. ABALLI, J. CABERA CALDERIN and J. M. L. SCULL, Arch. de med. inf. **8**:64 (March) 1939.

In a series of 30 infants with gonorrheal vulvovaginitis, 16 were treated with sulfanilamide and 14 by other accepted methods. The dose of the drug was 0.6 to 1 Gm. per 10 pounds (4.5 Kg.) of body weight per day. In the group thus treated 75 per cent were cured (bacteriologically) in an average of twenty-five and six-tenths days, while in the group on other therapy only 28.5 per cent were cured in an average of ninety-six days. Subsequent series of treatments should be given after a rest period, but not over a maximum of three.

SANFORD, Chicago

ANASARCA DUE TO NEPHROSIS AND INTERCURRENT ERYSIPELOID CUTANEOUS LESIONS. A. CASAUBON and S. CASSOY, Arch. de pediat. d. Uruguay **9**:516 (Aug.) 1938.

Casaubon and Cassoy present a case of anasarca of five months' duration in an 11 year old girl, due to a mixed kidney involvement (nephrosis being the more pronounced). Different therapeutic measures gave no relief. One and one-half months after her admission to the hospital extensive erysipeloid dermatitis developed. The bacteriologic findings were negative. The anasarca diminished, and the patient gradually improved.

SCHLUTZ, Chicago.

TREATMENT OF ACUTE NEPHRITIS IN INFANTS. F. DE FILIPPI, Arch. de pediat. d. Uruguay **9**:574 (Sept.) 1938.

De Filippi presents 7 cases of acute nephritis with favorable results. He recommends the method of starvation suggested by Volhard and claims that starvation and thirst prevent cardiac failure and uremia, shorten the course and prevent the development of the chronic form. He suggests that the weight, fluid output and arterial tension be carefully watched.

SCHLUTZ, Chicago.

RENAL ADENOSARCOMA AND SUBCUTANEOUS ELIMINATION PYELOGRAPHY. J. R. DREYFUS, Jahrb. f. Kinderh. **147**:12 (June) 1936.

A 5 month old child suffered from anorexia, vomiting, loss of weight and high fever. A large abdominal mass was palpated. Roentgenographic studies of the intestinal tract and pyelographic study following subcutaneous administration of perabrodil (skiodan) confirmed the impression of a tumor of the right kidney. Transperitoneal removal of the tumor (found to be adenosarcoma) was followed by shock and death. A plea is made for earlier diagnosis, the use of pyelography and, if necessary, instrumentation.

LANDAU, Hannibal, Mo.

Diseases of the Ductless Glands; Endocrinology

URINARY THYROTROPIC HORMONE. K. EMERSON JR. and W. C. CUTTING, Endocrinology **23**:439 (Oct.) 1938.

Urinary thyrotropic activity could not be demonstrated in normal persons or normal animals and only rarely in persons with hyperthyroidism. Transient urinary thyrotropic activity regularly followed thyroidectomy in animals and in man but only rarely could be demonstrated in spontaneous hypothyroidism.

JACOBSEN, Buffalo.

EFFECT ON THE GROWTH RATE OF THYRO-PARATHYROIDECTOMY IN NEWBORN RATS AND OF THE SUBSEQUENT ADMINISTRATION OF THYROID, PARATHYROID AND ANTERIOR HYPOPHYSIS. T. N. SALMON, Endocrinology **23**:446 (Oct.) 1938.

In newborn rats thyroparathyroidectomy resulted in severe retardation of growth. After three weeks the weights of these animals remained at about 25 to 35 Gm. The feeding of thyroid powder, beginning at weaning time, did not result in complete repair of this defect of growth.

Those given injections of parathyroid, beginning with the time of operation, showed a growth curve not significantly different from those which were left untreated after operation. A normal growth response was not obtained when newborn thyroparathyroidectomized rats were given thyroid alone beginning at the time of operation. Normal growth curves were obtained when they were fed thyroid and given injections of parathyroid.

Pituitary gland implanted in newborn thyroparathyroidectomized rats after weaning time did not produce a growth response if the animal was completely thyroidectomized. Only when thyroid remnants were demonstrable was a growth response noted.

JACOBSEN, Buffalo.

EXCRETION AND FATE OF ANDROGENS. C. D. KOCHAKIAN, Endocrinology **23**:463 (Oct.) 1938.

The subcutaneous injection of 10 different androgens into 1 normal and 4 castrate dogs did not result in excretion of estrogens in the urine as determined by the Allen-Doisy rat and mouse vaginal smear method. It seems that the male animal is unable to convert androgen to estrogen. The presence of the latter material in the male organism is due in part probably to independent production of the substance by the testis. The remainder is derived from some extragonadal source.

JACOBSEN, Buffalo.

INHIBITION OF LACTATION DURING THE PUERPERIUM BY TESTOSTERONE PROPIONATE. R. KURZROK and C. P. O'CONNELL, Endocrinology **23**:476 (Oct.) 1938.

Twenty-one patients who showed early lactation during the puerperium were treated with testosterone propionate for the purpose of inhibiting lactation. Usually inhibition of this function by the generally used therapeutic measures, and especially inhibition which occurs in the absence of therapeutic measures, is associated with pain, tenderness, engorgement and lumpiness of the breasts. Such conditions of the breasts require considerable nursing care and are very distressing to the patient. Testosterone propionate in doses of 25 mg. usually relieves such symptoms in about twenty-four hours without the addition of any other therapeutic measures.

JACOBSEN, Buffalo.

EFFECT OF ANTUITRIN S ON THE THYMUS OF THE YOUNG ALBINO RAT. E. O. BUTCHER and E. C. PERSIKE JR., Endocrinology **23**:501 (Oct.) 1938.

When injected into the young albino rat, the gonadotropic substance obtained from the urine of pregnant women (antuitrin S) caused an arrest of growth of the thymus. This effect could not be induced before the eighteenth day and was brought about via the gonads, since no such effect could be induced in gonadectomized animals. With continued injection of 20 units daily the effectiveness of the substance declined in the females. The changes induced in the thymus had no effect on the body growth of the animal.

JACOBSEN, Buffalo.

EFFECT OF YEAST AND OF THIAMIN ON THE PRODUCTION OF LOW IODINE GOITER. P. L. HARRIS and R. E. REMINGTON, J. Nutrition **17**:31 (Jan.) 1939.

Harris and Remington tested the conclusions published by Carpenter and Sharpless (*J. Nutrition* **13**:235, 1937) and could not substantiate the statement of these investigators that dried brewers' yeast is effective in influencing the size or the iodine content of the thyroid gland in the rat fed a low iodine, goiter-producing diet. The yeast-fed rats possessed glands equal in size, in dry matter and in iodine content to those of animals receiving autoclaved yeast, alone or supplemented with thiamin. The data show that vitamin B cannot be a substitute for iodine in preventing low iodine goiter.

FREDEEN, Kansas City, Mo.

ROLE OF IODINE (POTASSIUM IODIDE) IN EXPERIMENTAL HYPERTHYREOIDISM. V. M. TRIKOJUS, M. J. Australia **1**:220 (Feb. 11) 1939.

Trikojus produced in guiea pigs a syndrome simulating human hyperthyroidism by giving them progressively increasing doses of a thyrotropic extract of the pituitary gland. Two of 4 animals died of the effects of the thyrotropic substance, but the other pair survived owing to administration of potassium iodide in doses comparable to those used in treating human hyperthyroidism. Complete details of the autopsies on the 4 animals are given. The most striking differences were found in the thyroid glands. The animals given the thyrotropic extract alone showed complete absence of colloid in the thyroid gland, whereas those given potassium iodide had 50 per cent of the alveoli of the gland distended with colloid. The favorable effect of the administration of iodine is reflected in the weights and physical condition of the animals as well as in the difference in colloid storage as found at autopsy.

GONCE, Madison, Wis.

A HEMATONEUROLOGIC SYNDROME WITH DISTURBANCE OF THE DEXTROSE METABOLISM FROM THYMICOPANCREATIC DYSFUNCTION. M. ORTOLANI, Lattante **9**:434 (Oct.); 463 (Nov.) 1938.

An infant ten days after birth began to have frequent daily convulsions, which persisted but for one remission to its death, at 5½ months of age. At the age of 2 months the baby was markedly anemic (erythroblastic type). Postmortem examination disclosed reticular-endothelial hyperplasia, cerebral atrophy (hydrocephalus), thymic atrophy and hyperplasia of the pancreatic island tissue. Sugar tolerance tests, the injection of epinephrine hydrochloride and the injection of insulin caused no very abnormal changes in the blood sugar.

HIGGINS, Boston,

INFLUENCE OF LECITHIN AND OF LUTEIN ON THE HYPOGLYCEMIC ACTION OF INSULIN. G. PAVAN and C. MORO, Riv. di clin. pediat. **36**:994 (Nov.) 1938.

Bioplastin, a product containing 5 per cent lecithin and lutein, was used in these observations. Lutein is a colored material obtained from egg yolk. It is quite similar chemically to xanthophyll. Blood sugar curves were determined for normal children following administration of 30 Gm. of sugar; four curves were determined for each child, as follows: (1) with sugar alone, (2) with injection of 3 cc. of bioplastin, (3) with injection of 3 units of insulin and (4) with injection of 5 cc. of bioplastin and 3 units of insulin. The curves were progressively lower in the order given.

The combination of injections of insulin and injections of bioplastin in the treatment of diabetic children resulted in prolongation of the insulin action without production of a hypoglycemic reaction.

HIGGINS, Boston.

COMA DUE TO EMOTIONAL HYPOGLYCEMIA IN A DIABETIC CHILD. M. RODRIGUEZ, Arch. de pediat. d. Uruguay **9**:501 (Aug.) 1938.

Rodriguez presents a case of diabetes of four years' duration in a 10 year old girl. She was put on a restricted diet and given insulin.

During a severe emotional upset she went into coma, and hypoglycemia was marked. After treatment the condition rapidly improved.

SCHLUTZ, Chicago.

TUMORS OF THE THYMUS AND THEIR ASSOCIATION WITH MYASTHENIA. R. A. OBIDITSCH, Virchows Arch. f. path. Anat. **300**:317, 1937.

Nine cases of tumor of the thymus are described. In 4 of the cases the growth was benign and was termed lymphoepithelial; the predominating cell was the small lymphocyte. In 5 cases the tumor was malignant and of the squamous

epithelial type; this type the author terms a malignant medulla cell tumor. Only the benign tumors were associated with myasthenia. The benign tumors, which retained the function of the thymus, secreted an excess of a thymic substance causing myasthenia. Whether it acted directly on the muscle, on the nervous system or on the metabolism has not been determined.

O. T. SCHULTZ. [ARCH. PATH.]

A CASE OF ADRENAL VIRILISM. J. H. SMIDT VAN GELDER, Maandschr. v. kindergeneesk. **7**:472 (Sept.) 1938.

This is a clinical description of adrenal virilism as observed in a girl 9 years old. No exploratory operation was performed.

VAN CREVELD, Amsterdam, Netherlands.

FREE DIET METHOD OF DEALING WITH DIABETES MELLITUS IN CHILDHOOD. J. H. VERHAVE, Nederl. tijdschr. v. geneesk. **82**:4197 (Aug. 27) 1938.

After a brief recounting of the histories of 3 children in whom diabetes mellitus was found in the first year of life, Verhave describes the case of a girl aged 12 months in whom the disease was discovered in the precomatose stage. After the diabetic coma which had developed was surmounted with insulin, dextrose and saline solution, the child was treated successfully for six months by the free diet method after Stolte; up to the present this girl has remained in good condition.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

PHYSIOLOGICAL SCOLIOSIS. J. G. KUHNS, Arch. Pediat. **55**:343 (June) 1938.

Physiologic scoliosis occurs in at least 5 per cent of the school population. It is caused by weakness, incoordination and unequal function of the supporting muscles of the trunks. The treatment should be directed first to the general health, with attention to nutrition and to adequate rest. Then training and exercise should be given. The treatment must be continued for at least three months after the disappearance of the curvatures.

ORR, Buffalo.

OSTEITIS TUBERCULOSA MULTIPLEX CYSTOIDES AND SARCOID LESIONS. A. E. CONNOLLY, Brit. J. Radiol. **11**:25 (Jan.) 1938.

In osteitis tuberculosa the pseudocystic areas are due to granulomas which replace the bony tissue and which at times may expand and even perforate the bony shell. Sequestrum formation is rare, periosteal reaction is absent, and joints are usually not involved. The small bones of the hands and feet are the most frequently involved. The bone changes are often associated with tuberculoid manifestations in the skin.

Boeck described "sarcoid" lesions as a generalized granulomatous disease appearing as disseminated small nodes, grouped large nodular forms or a diffuse infiltration. The lesions predominate in the lymphatic system, lymphatic glands, tonsils and bone marrow, in the spleen, lungs and liver and also in the skin, where the dermatoses are recognized as Boeck's sarcoids. The lesions may be associated with tuberculosis, leprosy or syphilis. The granulomatous tissue, originating in the medulla, slowly permeates the bone, thereby producing various roentgenologic changes, depending on the extent of the change. Cystlike areas are usually located in the heads of the bones, are clearly defined, are round, oval or heart shaped. The cavities may be central or peripheral. When they are peripheral, there is a localized distention of the bone in which erosion of the thin shell may produce a large cavity continuous with the soft parts. There is another, "Grille type" which

is an exaggerated form of the diffuse type already mentioned. The lungs may be the site of abundant infiltrations about the bronchi and blood vessels. Sarcoid appears to be an infectious granuloma, occupying a place between tuberculosis and leprosy. Three cases are reported. In case 1, that of a 2 year old girl, there were tuberculous dactylitis, involvement of the radius, ulna, humerus and lower jaw and calcification of the intrathoracic glands. In case 2, that of a girl 16 years of age, there was tuberculosis of the dorsal spine. In case 3, that of a woman of 34 years, there were nodules on the hands and forearms, cystic changes in the hands and feet, increased hilar shadows and nodular infiltrations in the central lung fields, and sarcoid.

SQUIRE, Chicago.

AGE ORDER OF EPIPHYSEAL UNION IN BENGALEE GIRLS. S. K. BASU and S. BASU, J. Indian M. A. **7**:571 (Aug.) 1938.

One hundred and thirty school children ranging from 3 to 19 years of age were examined, and about 1,300 roentgenograms were taken. The degree of union of the epiphysial center with the diaphysis was divided into three stages: (1) non-union—when there is a clear space between the epiphysis and diaphysis; (2) intermediate union—when the epiphysial space is partly filled by bone; (3) complete uinon—when no space is seen between the epiphysis and diaphysis, and continuous bony strands are seen to pass from the one to the other. An epiphysial scar may remain for a long time after completion of fusion, but this must not be confused with earlier stages of fusion.

The findings may be summarized as follows:

Epiphyses	Age of Union in Majority of Bengalee Girls, Yr.
Proximal, humerus	16 to 17
Lateral epicondyle with shaft of humerus	12 to 13
Trochlea with shaft of humerus	12 to 13
Compound center for lower epiphysis with shaft of humerus	12 to 13
Medial epicondyle of humerus	13 to 14
Proximal, radius	13 to 14
Proximal, ulna	13 to 14
Distal, radius	16 to 17
Distal, ulna	16 to 17
Pisiform, center present at	11 and upward
Base, first metacarpal	14
Distal phalanx, thumb	13 to 14
Head, femur	13 to 14
Lesser trochanter, femur	13
Greater trochanter, femur	14
Distal, femur	16
Proximal, fibula	16 to 17
Proximal, tibia	15 to 16
Distal, fibula	15
Apophysis, calcaneous	14 to 15

TENNEY, Madison, Wis.

GENERALIZED OSSEOUS DYSTROPHY. E. SORREL and LE GRAND-LAMBLING, Bull. Soc. de pédiat. de Paris **36**:86 (Feb.) 1938.

A pale, undernourished 2 year old girl had multiple bony deformities. All the bones showed osteoporosis and periosteal thickening. In spite of negative serologic tests, antisyphilitic treatment was instituted. The blood showed no evidence of erythroblastosis.

BENJAMIN, Montreal, Canada.

PAROXYSMAL MYOPATHIC CRISES WITH HEMOGLOBINURIA. J. HUBER, J. FLORAND, J. A. LIÈVRE and NÉRET, Bull. Soc. de pédiat. de Paris **36**:96 (Feb.) 1938.

A boy 4 years old had spasm of the muscles of the lower extremities. The feet were held in the position of talipes equinus, and any attempt to move them elicited pain. This condition was accompanied by fever and hemoglobinuria. Rales were present in the lungs. There were no positive neurologic findings. A similar condition of myositis with hemoglobinuria has been observed in horses.

BENJAMIN, Montreal, Canada.

MANAGEMENT OF GENERALIZED OSTEITIS FIBROSA. O. TIMPE, Beitr. z. klin. Chir. **164**:146, 1936.

A 14 year old girl had severe osteitis deformans associated with disturbances of other organs of internal secretion. No parathyroid tumor was found on operation. Ligation of the inferior thyroid arteries was performed, with improvement in the condition of the patient.

RUBIN, Boston.

A CASE OF THE KLIPPEL-FEIL SYNDROME. A. VAN WESTRIENEN, Maandschr. v. kindergeneesk. **7**:486 (Sept.) 1938.

This is a description of the Klippel-Feil syndrome as seen in a girl of 8 years, with a short discussion of the genesis of the disease.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF PRIMARY CHRONIC INFECTIOUS ARTHRITIS. J. H. VAN GORTEL, Nederl. tijdschr. v. geneesk. **82**:3977 (Aug. 13) 1938.

Van Gortel reports the occurrence of primary chronic infectious arthritis in a girl nearly 2 years old.

VAN CREVELD, Amsterdam, Netherlands.

SOME REMARKS ON PERTHES' DISEASE, ESPECIALLY WITH REGARD TO TREATMENT. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **82**:4962 (Oct. 8) 1938.

The cause of osteochondritis juvenilis coxae is yet unknown. Harrenstein shows that in this condition, besides destruction and necrosis in the head of the femur, a productive process is also present, revealing itself by enlargement of the proximal epiphysial disk of the femur. The roentgen picture of the diseased joint cannot but inform one incompletely about the degeneration of the bone tissue and the supporting power of the head of the femur, as decalcified areas on the picture are caused in various ways.

An after-examination of 14 patients who had been treated only by recumbency and plaster cast for the time that pain and stiffness of the joint made this treatment unavoidable showed that in half of them a well nigh ideal healing had taken place with regard to both the form of the femur head and the function of the joint. The therapeutic value of more radical methods of treatment can only be assessed, therefore, from reports of the results in a large series of patients.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

EXTERNAL DISEASES OF THE EYE IN SCHOOL-CHILDREN. A. FURNISS, Practitioner **141**:771 (Dec.) 1938.

"The commonest eye diseases which the school medical officer has to deal with in the minor ailment clinics are blepharitis, conjunctivitis, keratitis, corneal opacities, and a great many other conditions, such as styes, tarsal cysts, foreign bodies

in the eye, and injury to the eye. The causation may be summed up as (*a*) dust and dirt, especially in the case of blepharitis and conjunctivitis; (*b*) infectious diseases, especially measles; (*c*) contagion, e. g. due to the use of towels in common; (*d*) injury, particularly likely to occur when numbers of children are playing together; (*e*) venereal diseases; both gonorrhoea and syphilis still remain among the important causes of blindness, and interstitial keratitis, though less frequent than formerly, is due almost solely to the latter disease; (*f*) errors of refraction."

In regard to general preventive measures, it may be said that if a child is "provided with a generous diet of satisfactory vitamin content, with a sufficiency of milk, with open-air conditions and with sufficient rest, there is little likelihood of the contraction of eye disease. Within the school persistent and vigilant attention to all matters connected with cleanliness are essential, whether of the building, equipment or playground. The children should be frequently inspected for cleanliness by the school nurses. There is still room for improvement in some schools in the poorer districts in regard to lavatory accommodation, the provision of hot water, the supply of towels and generally the facilities afforded to the children in the use of the provision made. It is important that the ophthalmic surgeon should study from every point of view this question of eye disease in any form in his area, note carefully its incidence, especially in relation to improvement or otherwise, satisfy himself about the kind, manner, and frequency of the treatment given, and in particular to advise in cases in which hospital or other form of residential provision is required."

GELSTON, San Francisco.

PIGMENTARY DEGENERATION OF THE RETINA AS A DOMINANT HEREDITARY CHARACTERISTIC. J. FRANÇOIS, Ann. d'ocul. **174**:403 (June) 1937.

In a study of 40 members of a family belonging to five generations, François found pigmentary degeneration of the retina in 13 persons (8 males and 5 females). No consanguinity was noted in this series.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

DISLOCATION OF THE OCULAR LENSES OF A PREMATURE INFANT. DOLICHOSTENOMELIA? P. NOBÉCOURT, J. CATHALA and TEMERSON, Bull. Soc. de pédiat. de Paris **36**:21 (Jan.) 1938.

A boy born prematurely at 6½ months was markedly underdeveloped at the age of 21 months. The lens of each eye was dislocated, an anomaly which is frequently associated with long, thin hands and feet. In this case only the feet were suggestive of dolichostenomelia (arachnodactylia).

BENJAMIN, Montreal, Canada.

IDIOCY WITH BLINDNESS DUE TO CONGENITAL CATARACTS IN TWO BROTHERS. M. HEUYER, BERNARD-PICHON and JOFFROY, Bull. Soc. de pédiat. de Paris **36**:92 (Feb.) 1938.

Two brothers, 7 and 12 years old, showed marked mental retardation and blindness practically from birth. Both had bilateral cataracts. A table of the geneology is given, demonstrating ocular deficiency on the maternal side. It is believed the anomalies in these children were congenital, though not of the Tay-Sachs type.

BENJAMIN, Montreal, Canada.

CONTRIBUTION TO THE ANATOMOPATHOLOGIC STUDY OF XEROPTHALMIA IN INFANTS. A. CASTELLANOS, Bol. Soc. cubana de pediat. **9**:383 (Sept.) 1937.

Castellanos has made a detailed study of the histopathologic changes in incipient keratomalacia. The tissue changes were mainly trophic lesions, and secondary infection did not play an important role.

He includes a description of the classic changes in experimental keratomalacia in mice.

SCHLUTZ, Chicago.

TREATMENT OF CONGENITAL ATRESIA OF THE NASOLACRIMAL DUCT. S. LARSSON, Acta ophth. **16**:271, 1938.

The nasolacrimal duct may be longer than the bony canal containing it. In such cases the duct continues below the orifice of the bony canal, the medial wall of the duct being covered by nasal mucous membrane. The normal opening of the duct may form a window on the medial wall above the end of the duct. For this reason there are certain patients with congenital atresia of the lacrimal duct who cannot be successfully treated by probing, for the probe passes to the floor of the nasal fossa without producing a perforation medially. In 2 such instances the author has removed the tip of the inferior turbinate and incised the mucosa against a probe which had previously been introduced in the usual way.

PERKINS, New York. [ARCH. OPHTH.].

FOUR SYNDROMES OF "PHAKOMATOSES." J. VAN DER HOEVE, Nederl. tijdschr. v. geneesk. **82**:4418 (Sept. 10) 1938.

A brief review is given of the symptoms that may supervene in the four syndromes belonging to the collective notion of "phakomatoses." The classification of the phacomas is in accordance with Albracht's for the genesis of tumors. A number of cases are described, among which are 2 cases of glioma retinae. One of the patients did not present signs of the glioma before the fifteenth year of life. The hereditary nature of phacomas is pointed out, and great importance is attached to the study of these growths not only as to their diagnosis and treatment but also as to the progress of knowledge in the field of cerebral changes and of the genesis of tumors.

VAN CREVELD, Amsterdam, Netherlands.

Skin Diseases; Allergy

ALLERGY IN CHILDHOOD: I. THE MODES OF ITS ACQUISITION. B. RATNER, J. Pediat. **12**:730 (June) 1938.

Ratner reviews the modes of acquisition of allergy. All persons are potentially capable of acquiring allergy. The capacity to become sensitized differs more largely because of quantitative than because of qualitative considerations. Antigens or antibodies may be transmitted to the fetus through the placenta. Unaltered proteins may pass through the walls of the digestive tract or the upper part of the respiratory tract. Unaltered allergens may enter the blood stream by way of the skin or in the course of treatment by parenteral injections. The acquisition of hypersensitiveness depends on: (*a*) constitutional or other factors peculiar to the patient; (*b*) the nature of the exciting substance; (*c*) the amount of antigen to which the patient is exposed; (*d*) the amount of native antigen which actually invades the blood stream; (*e*) the intervals at which such exposures occur.

RAUH, Cincinnati.

ALLERGY IN CHILDHOOD: II. PROPHYLAXIS. B. RATNER, J. Pediat. **12**:737 (June) 1938.

Ratner presents suggestions on the management and care of the normal infant for possible prevention of allergic disease. To avoid intrauterine sensitization to any food, a varied diet should be prescribed for the pregnant woman; a portion

of the food should be given in "allergenically-denatured" form. Overeating should be discouraged and the mother warned especially against excessive indulgence of an appetite for any single protein food. Ratner believes that newborn infants who are given cow's milk during the first two weeks of life and then put on breast milk entirely may become sensitized to milk, which is not evidenced until weaning is attempted. To avoid this, some form of "allergenically-denatured" milk in conjunction with some denatured form of carbohydrate should be used in the feeding of newborn infants until breast feeding is completely established. During diarrhea increased permeability of the intestinal wall may occur permitting entrance of unchanged protein into the blood stream. At this time "allergenically-denatured" foods and a varied diet should be given and new foods avoided. A similar condition of the intestinal tract is present during convalescence from other illnesses, and the same precautions must be taken. Excess of any food, fad diets and the introduction of new foods early in infancy should be avoided. Sensitivity to dust may be avoided if the nursery is kept as free as possible from dust and furnishings which produce dust. Prevention of infections, particularly those of the upper respiratory tract, and infectious diseases, with use of all available methods of immunization, may aid in the prevention of "bacterial allergy." The control of drug and serum therapy will aid in the prevention of hypersensitivity to both.

RAUH, Cincinnati.

DIETETIC TREATMENT OF "ECZEMA" IN EARLY INFANCY. L. W. HILL, New England J. Med. **217**:690 (Oct. 28) 1937.

Seborrheic Dermatitis.—György, of Heidelberg and Cleveland, has advanced the theory that seborrheic dermatitis is caused by lack of a vitamin hitherto unknown, which he calls vitamin H, in combination with toxicity from absorption of unsplit lactalbumin. The vitamin is found in liver, potatoes, casein and yeast. Regardless of whether the theory is correct, the corresponding therapy often works. A formula rather low in fat and sugar with addition of precipitated casein is likely to give good results.

Contact Dermatitis.—Scratch or intracutaneous tests are negative; patch tests may be positive. This dermatitis has nothing to do with diet.

Fungus Infection.—In infants fungus infection is more likely to be due to the yeastlike group of organisms, particularly Monilia albicans, the organism of thrush, than to the Trichophyton group, which is the commonest offender in adults. Fungus infections are most likely to occur around the genitalia and buttocks or in the groins but may be found on any part of the body. In order to diagnose a fungus infection accurately, pathogenic fungi must be recovered from the lesions, either by culture or by direct scrapings. M. albicans thrives on carbohydrates; therefore a diet low in carbohydrate is indicated.

It is in cases of atopic dermatitis that diet may be of the greatest importance, and most cases of "eczema" in infancy belong to this group.

Most infants when they begin to have eczema are being fed nothing but cow's milk, orange juice and fish oil. Most allergists have found that even if sensitivity to fish is present the patient may take the corresponding oil with impunity.

The scratch test with protein obtained from oranges is rarely positive. It was positive in only 4 of 300 eczematous infants and children. The direct intracutaneous test is more often positive; in 22 children under 1 year of age tested by this method there were 8 positive reactions. If orange juice is omitted, crystalline vitamin C should be substituted.

The milk in the diet is the most important constituent to consider. Of 153 children under 1 year of age on whom scratch tests were made with casein or lactalbumin, only 17 per cent had positive reactions. But in another series of 64 children under 1 year of age in whom scratch tests were negative, 56 per cent reacted positively to intracutaneous tests with lactalbumin.

There are three dietary possibilities in dealing with sensitivity to milk: 1. Heated milk may be used. 2. Goat's milk may be used. 3. Milk may be withdrawn entirely and a milk-free food substituted. It is not certain how common sensitivity to casein is, but it has been thought to be much less so than sensitivity to lactalbumin. It must be remembered that in heated milk the allergenic power of the lactalbumin has not been entirely done away with; it has merely been reduced.

The lactalbumins of goat's and cow's milk are biologically different. If sensitivity to casein is present, goat's milk is not indicated. If sensitivity to lactalbumin alone is present, goat's milk is indicated and is likely to be much more efficacious than evaporated cow's milk. In eczema Hill has been able to get much better results with a milk-free diet than with either heated cow's milk or goat's milk.

Of the cereals, wheat gives positive skin reactions most frequently.

Sensitivity to egg is so common that it may be said to exist in most of these infants. But egg protein has not produced the eczema, for most of them have never eaten eggs. The sensitization is probably of intrauterine origin. As a rule, eggs should not be included in the diet of an eczematous infant.

Of the vegetables, spinach and peas frequently give positive skin reactions. String beans and carrots rarely do so. These are therefore the best vegetables to use.

Hill has never seen a positive skin reaction to banana protein in an infant, nor has he seen banana aggravate an eruption.

GENGENBACH, Denver.

EPIDERMOLYSIS BULLOSA. T. COLVER, Proc. Roy. Soc. Med. **31**:1123 (July) 1938.

Epidermolysis bullosa is reported in a girl of 2 years. She was the sixth child. The other children were alive and well. On examination all the fingers and a considerable area of the hands were red. The confluent area had a sharp margin, contrasting markedly with the normal skin. The feet were similarly affected. The color was due to dilatation of the vessels in the skin and was obliterated by pressure. There was frequent blistering of the reddened skin. Fluid from the vesicles was sterile. The child was very backward; she could not stand; her habits were unclean; she could not speak and was not able to sit up until the twenty-fourth month. Investigations all gave negative results.

WILLIAMSON, New Orleans.

DERMATOMYOSITIS COMPLICATED BY CALCINOSIS. R. H. BAILEY, Proc. Roy. Soc. Med. **31**:1153 (Aug.) 1938.

The case reported was that of a girl of 12 years. She was first taken to England in 1930 from Switzerland. At the age of 4 swellings developed on the hands and feet, resembling chilblains. They persisted until she returned to Switzerland some months later. On her return to England in 1935 they recurred. When cold her hands felt "burning on the inside." The symptom disappeared on her return to Switzerland. In 1936 she was taken to live in England. Difficulty in bending was noticed first; then stiffness began in the back and legs and then in the arms. Also on examination the subcutaneous tissue was found to be markedly thickened. A roentgenogram showed large calcium deposits apparently attached to the upper margins of both acetabulums. The great opacity of the involved areas suggested that ossification was taking place. This observation is unusual in dermatomyositis. A little calcium deposit was seen external to the left knee joint. A reproduction of the roentgenogram and a report of the chemical examination of the blood accompany the report.

WILLIAMSON, New Orleans.

ERUPTIVE FEVER (DENGUE, MEASLES, GERMAN MEASLES)? IN REALITY, COMPLEX TOXIC DRUG DERMATITIS (PENTAVALENT ARSENIC AND SULFANILAMIDE DERIVATIVE). G. BLECHMANN and R. C. FRANÇOIS, Bull. Soc. de pédiat. de Paris **36**:51 (Jan.) 1938.

A child who had been in Beirut suffered from a febrile illness which was accompanied by an eruption of the skin. Blechmann and François discuss the differential diagnosis, mentioning dengue, measles and rubeola as well as the possibility of toxic dermatitis following administration of acetarsone (stovarsol) and sulfanilamide. No definite conclusion is reached. It is said that derivatives of sulfanilamide are being used in unbelievable quantities (several tons weekly) in the United States, and a word of warning is sounded that the enthusiasm for the use of this new drug should be tempered by a realization of its possible toxic effects.

BENJAMIN, Montreal, Canada.

INHERITANCE OF NEUROFIBROMA (RECKLINGHAUSEN). C. H. SCHRÖDER, Beitr. z. klin. Chir. **164**:563, 1936.

On investigation of one family Schröder encountered some light, abortive forms of this disease. This should encourage other physicians to continue investigation along these lines.

RUBIN, Boston.

INVERSE ANAPHYLAXIS IN MAN; PROBLEM OF HYPERSENSITIVITY IN MAN. E. A. Voss, Ztschr. f. Kinderh. **59**:612 (April 2) 1938.

Voss discusses allergy, anaphylaxis and idiosyncrasy at some length. Anaphylaxis is generally regarded as an antigen-antibody reaction. Although the antigen-antibody reaction can be demonstrated in vitro, the substance causing anaphylaxis in vivo is not produced. In experiments on animals a definite period of latency antedates the development of anaphylaxis. Anaphylactic manifestations are more complicated in man than in experimental animals. Occasionally anaphylaxis is observed without any apparent period of latency, and some American authors, especially Cooke, have ascribed greater importance to hereditary than to acquired anaphylaxis. However, sensitization may result via the gastrointestinal or the pulmonary route.

Inverse anaphylaxis is a form of anaphylaxis which develops without a period of latency on injection of a serum containing antibody after injection of antigen. Voss studied this phenomenon in children by injecting serum from persons convalescent from serum sickness into children to whom antidiphtheritic serum had been administered, on different days following the administration, and also at the beginning of serum sickness, at its height and at the time of subsidence of the exanthem. Reactions could be produced at any time during the period of incubation of serum sickness, and the severity of the manifestations was closely related to the time of injection. Reactions always began at the site of injection of the antidiphtheritic serum. Voss hopes to answer the question why serum reactions occur naturally in only about 20 per cent of cases, whereas experimentally they can be produced consistently in man. In animals inverse anaphylaxis is much less readily demonstrated.

He discusses the significance of inverse anaphylaxis, especially as regards transfusion. Desensitization by means of inverse anaphylaxis may be possible. With slight variation in technic the presence of antibodies in man can be demonstrated.

SIEMSEN, Chicago.

Miscellaneous

STUDIES ON THE MECHANISM OF THE ACTION OF SULFANILAMIDE. J. S. LOCKWOOD, A. F. COBURN and H. E. STOKINGER, J. A. M. A. **111**:2259 (Dec. 17) 1938.

Two hundred and fifty patients were treated with sulfanilamide for various infectious conditions. A careful review is made of their records. The doses

were maintained at a level sufficient to give a blood concentration of 50 micrograms per cubic centimeter. Fifty per cent of the adults and 20 per cent of the children showed some toxic reaction, but no deaths resulted from treatment with this drug. The incidence of each reaction is given, including the mild types (cyanosis, gastrointestinal and nervous symptoms, fever, precordial and abdominal pain, and acidosis), the more severe reactions (rash, jaundice, anemia, hemoglobinuria and granulocytopenia) and secondary and late reactions. The reaction had no relation to the therapeutic effect.

All types of hemolytic streptococci were found amenable to treatment. In many patients recrudescences were seen after withdrawal of the drug, especially if the focus was in necrotic tissue. In well developed abscesses free surgical drainage was necessary along with sulfanilamide therapy. When staphylococci were present in these abscesses, they were not inhibited, and their activity decreased the effect on the streptococci present.

Sulfanilamide was most effective in infections of the blood and soft tissues; it was not so effective in bone or in regions of extensive destruction of tissue. Determinations of the formation of antibodies for streptococci during treatment revealed that sulfanilamide had no effect on the formation of such defenses.

Not only did the type of organism present determine the effect of treatment but also its situation and the type of lesion. The drug definitely limited the invasive power of certain bacteria. The effect in scarlet fever, tonsillitis, sinusitis, otitis and mastoiditis was questionable.

HEERSMA, Kalamazoo, Mich.

ACTUAL SITE IN SKIN OF INTRADERMAL INJECTIONS. F. W. TAYLOR, J. A. M. A. **111**:2475 (Dec. 31) 1938.

Study of sections of skin into which india ink had been injected in the recognized manner revealed that in intradermal injections material is injected much deeper than is generally believed, i. e., in the dermis at variable depths and not in the epidermis.

HEERSMA, Kalamazoo, Mich.

MERCURIAL POISONING FROM BICHLORIDE OF MERCURY ENEMA. A. M. SCHWITTAY, Wisconsin M. J. **37**:550 (July) 1938.

In treatment for pinworms, a 10 year old girl was given an enema containing 7½ grains (0.48 Gm.) of mercury bichloride. Symptoms were noted within two hours: severe abdominal pain and tenderness, blood stained vomitus and stools, weakness, pallor and acute nephritis. Complete anuria developed the second day and lasted twenty-four hours. There were stupor, edema and persistent vomiting. The fourth day an 8 inch (20 cm.) mucus cast of the intestine was passed. The girl was discharged on the tenth day and was completely recovered only after three months. The treatment consisted in the use of the usual supportive measures and administration of sodium thiosulfate.

JANNEY, Wauwatosa, Wis.

THE USE OF FEVER THERAPY IN CHILDREN. M. D. FERDERBER, Brit. J. Phys. Med. **1**:219 (June) 1938.

The use of fever in the treatment of children for chorea is discussed at length. It is believed that there is a tendency to undertreat these patients. In the author's experience, the patients receiving eight to ten treatments of no less than three hours each made the greatest improvement. A routine preparation for fever treatment is outlined, and a few brief case reports are given.

HARTMAN, Cleveland.

TOXIC SYNDROME IN CHILDREN. L. RIBADEAU-DUMAS, Bull. Soc. de pédiat. de Paris **36**:187 (April) 1938.

The toxic syndrome observed in children with acute infection, sunstroke, heatstroke and especially anaphylactic shock resembles that encountered in children with eczema. It is characterized by stupor, pallor, hyperpyrexia, vomiting, diarrhea and dehydration, a complex of symptoms not unlike that observed in infants with severe dysentery. There is vascular hyperemia and edema of the organs, which are believed to be related to a neurovegetative disturbance, possibly associated with the function of the cortex of the adrenal.

BENJAMIN, Montreal, Canada.

ADVICE ON THE REGULATIONS OF LABORATORY TECHNIC. A. SELLEK AZZI, Arch. de med. inf. **8**:394 (Sept.) 1938.

In view of the necessity of establishing in Cuba courses of study looking toward the development of technics for clinical laboratories, the author is collecting data as to the regulation of such laboratories in the United States. It is requested that any communications along this line be sent to the University of Habana Medical College, so that such educational courses may be established along appropriate and practical lines.

SANFORD, Chicago.

TREATMENT OF CAUSTIC (LYE) POISONING IN THE CHILDREN'S CLINIC OF THE UNIVERSITY OF BUDAPEST. E. GYÖRGY, Pract. oto-rhino-laryng. **1**:203 (July) 1938.

György has shown that the many laws prohibiting the indiscriminate sale of lye and other caustics have markedly decreased the number of patients with caustic poisoning admitted to this station. In 1923, 122 patients were admitted; in 1936, only 19.

The method of treatment is bougienage beginning five to six days after the poisoning. The author uses a soft rubber sound, the gage of which varies with the age of the patient: under 1 year, no. 28; between 1 and 3 years, no. 29, and over 3 years, no. 30 or 31. The sound is warmed in hot water and lubricated with liquid petrolatum before insertion. After its induction, the gag is removed and a small rubber stopper slipped over the sound. This rests between the teeth. For the first six weeks the sound is permitted to remain in place for fifteen minutes. After eight weeks it remains only five minutes. If the patient responds to this treatment, a semisoft sound with a conical end (Rusch) is substituted. If fever or evidences of bleeding occur, the bougienage is continued with a sound of smaller caliber. If difficulties are encountered in the use of the sound or the patient is seen several weeks after the poisoning, then a fine probe must be used. This procedure is perhaps best done by esophagoscopy, by means of which one can determine definitely the degree and position of the stricture. After the probe has been passed, the dilation can be continued by a suitable sound. If the stricture is so marked that the child can swallow only water and the sounding is practically impossible, gastrostomy is indicated, which in a few weeks should be followed by retrograde bougienage.

The success of the treatment depends on its continuance over a long period.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

Society Transactions

AMERICAN PEDIATRIC SOCIETY

CLIFFORD G. GRULEE, M.D., *President*

Annual Meeting, Skytop, Pa., April 27-29, 1939

HUGH MCCULLOCH, M.D., *Secretary-Treasurer*

First Session

Thursday Afternoon, April 27

THE NEWBORN: PRESIDENT'S ADDRESS. DR. CLIFFORD G. GRULEE, Evanston, Ill.

This paper was published in full in the July issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 1.

PRODUCTION OF PASSIVE IMMUNITY AGAINST INFLUENZA VIRUS BY INTRODUCING IMMUNE SERUMS INTO THE RESPIRATORY TRACT. DR. JOSEPH STOKES JR. and DOROTHY R. SHAW (by invitation), Philadelphia.

Immune serum was obtained from mice after three intraperitoneal injections of a 10 per cent suspension of mouse lung infected with the PR-8 strain of virus. In neutralization tests their pooled serum gave complete protection to mice in a dilution of 1:320 when mixed with an equal portion of a 2 per cent suspension of glycerinated mouse lung infected with PR-8 virus.

Immune rabbit serum was obtained similarly, except that in addition to intraperitoneal injections of infected mouse lung intravenous injections of tissue culture PR-8 vaccine were given. The immune titer was the same as that of the mouse serum. The human immune serum used was a pool from 5 persons who had received intramuscularly increasing weekly doses of tissue culture vaccine, consisting of seven strains of human influenza virus. Neutralization tests on these serums will be reported later.

Immune ferret serum was obtained from a ferret which had recovered from infection with the Philadelphia 37-9 strain of virus. The titer of neutralizing antibodies in this serum was 1:160.

Normal rabbit serum with no neutralizing antibodies was used for the control studies.

Groups of 8 mice each were given intraperitoneal injections of the normal rabbit serum, anti-PR-8 rabbit serum and immune human serum, respectively, at varying intervals. One hundred thousand minimum lethal doses of PR-8 virus was instilled intranasally, with the subjects under ether anesthesia, two hours and one-half hour after the injection of the immune serum. Two other groups of 8 mice each were given serum in the same manner, one group receiving it two hours and the other six hours after the intranasal injection of the virus.

None of these mice showed any evidence of protection against the PR-8 strain of influenza virus, owing possibly to the large amount of virus in the dose used to test immunity.

Groups of 10 mice were given anti-PR-8 mouse serum intranasally, without anesthetization, at varying intervals. One thousand minimum lethal doses of PR-8 virus was instilled intranasally, with the subjects under ether anesthesia,

forty-eight, twenty-four, ten and two hours and one-half hour after the injection of the immune serum. There was no significant difference between these mice and controls receiving nonimmune serum.

Groups of 8 etherized mice were given intranasally 0.05 cc. of normal rabbit serum, anti-PR-8 rabbit serum and immune human serum, respectively, six and two hours and one-half hour before the instillation of 100,000 minimum lethal doses of PR-8 virus. The mice which received the anti-PR-8 mouse serum two hours and one-half hour before virus was instilled all survived. Unfortunately, the supply of the immune mouse serum became exhausted before completion of testing of all the groups of mice. The tests are being repeated and will be reported later. The mice receiving the normal rabbit serum all succumbed, as did the controls. Practically all of the mice survived when anti-PR-8 rabbit serum and immune human serum had previously been injected intranasally.

One ferret under ether anesthesia was given an intranasal injection of immune ferret serum twenty-four hours before the intranasal injection of Philadelphia 37-9 virus. A second ferret under ether anesthesia received virus alone. The ferret receiving the immune serum survived with practically no symptoms, whereas the ferret receiving virus alone died in four days.

Whether the passive immunity produced by the immune serums used was due to rapid absorption of antibodies into the circulation or to direct attachment of antibodies to the cells of the respiratory tract is still a subject for study. It appears improbable that unabsorbed antibodies were responsible. The more solid immunity produced by homologous immune serums suggests better absorption of such serums.

CLINICAL AND EXPERIMENTAL STUDIES OF LIPOID PNEUMONIA. DR. IRVING J. WOLMAN (by invitation), Philadelphia.

Lipoid pneumonia has been defined as the chronic pneumonia which follows the entrance of fats or oils into the lungs. Certain problems were encountered in a study of 65 human patients. Milk aspiration pneumonia was not included.

In 20 of these cases the diagnosis was not made until after death, when characteristic infiltrations were noted at necropsy. The exogenous origin of the oil was demonstrated by the topography of the lesions. Pathologic identification of the offending lipoid can usually be made by special histologic technics. I observed that the pneumonic areas fluoresce in ultraviolet radiation, especially after fixation with a solution of formaldehyde.

Experimental pneumonia can be produced in rabbits by intranasal instillation of liquid substances. I have studied the microscopic and fluorescent characteristics of involved areas in five groups of involved rabbit lungs. The substances used were cod liver oil, liquid petrolatum, butter, evaporated milk and fat-free milk. Evaporated milk and fat-free milk produce an acute inflammatory reaction which resolves completely except for residual scars. Butter is quickly phagocytosed and removed. Liquid petrolatum remains as an inert phagocytosed foreign body. Cod liver oil gives rise to an acute necrotizing reaction which later heals in the form of chronic fibrosis encircling amorphous material. These types of aspiration pneumonia are individual and distinctive for the substances tested; each originates a characteristic cycle of changes.

From the outpatient department and wards of the Philadelphia Children's Hospital 45 additional cases were collected, in 30 of which the condition was recognized in the past eight months. Diagnostic criteria were (*a*) history of ingestion of oil, (*b*) characteristic roentgen appearances, (*c*) chronicity of lesions as demonstrated in repeated roentgen examinations, (*d*) absence of other pulmonary diseases and (*e*) a negative tuberculin reaction. Offending oils have been chiefly liquid petrolatum, cod liver oil or both. There are usually no symptoms and signs except when the onset is sudden and accompanied by acute pulmonary reactions. Affected children are usually susceptible to recurrent infections of the upper respiratory tract. The prognosis for life is good, although the shadows in

the lungs usually persist for at least several years. A good proportion of the children have or had predisposing debilitating diseases. Infancy is the age period in which entrance of oil usually takes place. Lipophages have been found in a few bronchoscopic specimens.

DISCUSSION

DR. HENRY J. GERSTENBERGER, Cleveland: Did you find in any of the cases of pneumonia that the heart was displaced to one side or the other as the result of subsequently developing atelectasis?

DR. CHARLES HENDEE SMITH, New York: Many points might be discussed. First, why are the shadows always hilar? One can make a diagnosis of lipoid pneumonia on the distribution of the shadows alone. I have always felt that this was due to the anatomic fact that the hilar lobules of the lung are supplied by recurved bronchi. The bronchial tree divides dichotomously like an elm tree, with recurving branches to the hilar lobules. It is not like a spruce tree, with right-angled branches going off and supplying the lobules adjacent to the large trunks. There is thus a mechanical factor in the smaller amount of free drainage from the hilar region.

I should like to emphasize the facts that aspirated milk does sometimes kill little babies and that the acute exudative inflammation which it causes does not always resolve. The same thing is true of cod liver oil. A number of fatalities have been due to aspiration of milk or of cod liver oil. It seems that this is a good argument for not giving cod liver oil to premature, very young or feeble infants, particularly those with congenital defects. To these babies vitamin D can best be given in the form of drisdol (purified vitamin D in propylene glycol).

The difficulty of obtaining the history of administration of oil is sometimes great. One child with a classic hilar shadow had not grown or gained normally. I made eight visits before I could get any history of administration of oil. I finally found that while the baby was in the hospital in the first two weeks the nurse had put petrolagar (liquid petrolatum emulsified with agar) into the bottle. It had floated down the wrong way or had been eructated and aspirated. There was definite lipoid pneumonia, but, as in many other cases, the difficulty of learning the history was extreme.

DR. BENJAMIN KRAMER, Brooklyn: In 1934 Dr. Lederer reported from the clinic with which I am associated a series of 6 cases of lipoid pneumonia with postmortem observations. In some of these cases the lung showed multiple areas of necrosis, with accumulation of lipophages in the alveoli.

This succession of mortalities impressed my co-workers and me with the seriousness of this condition.

More recently we have seen a series of 6 patients with chronic pneumonitis from whom we were unable to obtain a history of aspiration or administration of oil; nevertheless, the roentgenograms so closely resembled those of lipoid pneumonia that we concluded that the condition in these cases also must be of this type. Of the latter 6 patients, 4 recovered. We followed some for three or four years and observed a gradual clearing up of the consolidation, which at times seemed to involve more than half of the entire pulmonary field.

After recovery the children were apparently normal both mentally and physically; hence I believe, as Dr. Wolman has indicated, that many of the children are initially normal.

Another important point is the absence of symptoms involving the respiratory tract early in the course of the disease. Physical examination of the lung fails to reveal any evidence of disease. There are undernutrition and marked anorexia and occasionally diarrhea, but only fluoroscopic or roentgenographic examination reveals, often to our surprise, an extensive shadow in the lungs. The presenting symptoms are often nutritional rather than pulmonary.

At times the clinician's attention is called to the malady because of superimposed secondary infection of the respiratory tract, which accentuates the clinical picture.

Complete resolution of the pulmonary process may take two or three years. We have not made bronchoscopic examination, but efforts to demonstrate lipophages in the sputum have been uniformly unsuccessful.

DR. LEWIS WEBB HILL, Boston: Dr. Wolman's paper is valuable and timely. I have never seen oily nose drops do good to a baby. I see no reason for putting anything up the nose of a baby with an ordinary acute cold. If the child has a postnasal infection with thick, stringy pus, gentle syringing with a mild saline solution is good treatment. Dr. Wolman has shown clearly that oily nose drops probably do no good and may do a great deal of harm.

DR. HAROLD L. HIGGINS, Boston: What chemical constituent of cod liver oil causes this reaction in the lung?

DR. IRVING J. WOLMAN, Philadelphia: The highly irritating substance in cod liver oil is either wax or unsaturated fatty acids. The anatomic distribution of the lesions in the lungs shows their exogenous origin. Oil collects in the same places as the foreign bodies which bronchoscopists endeavor to locate. The fact that in the less advanced stage the lesions lie in the central regions of the lungs explains the absence of physical signs in many patients. A band of uninvolved, air-containing parenchyma separates consolidation from the wall of the chest.

Bronchoscopic treatment proved valueless. The quantity of obtained secretion was small. On searching for sputum in gastric washings, one finds a great deal of material derived from the nose and throat, which confuses the picture. It is hoped that the ultraviolet microscope will assist in the detection of the globule-containing cell. It is often stated that aspirated milk can give rise to chronic pneumonia; however, in animals which received milk my associates and I found no striking residue of chronic inflammation. Displacement of the heart was not observed in any of our cases.

TREATMENT OF PNEUMOCOCCIC INFECTIONS IN CHILDREN WITH SULFAPYRIDINE.
DR. HENRY S. CHRISTIAN (by invitation), and DR. GILBERT M. JORGENSEN (by invitation), New York.

This paper will be published in full, with discussion, in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

SERUM TREATMENT OF PNEUMONIA DUE TO PNEUMOCOCCUS TYPE XIV.
DR. EDWARD C. CURNEN JR. (by invitation), Boston.

From Jan. 1, 1937, to Jan. 1, 1939, pneumococci were isolated from 608 patients under 12 years of age, of whom 120, or 19.7 per cent, yielded Pneumococcus type XIV, the most frequent single type encountered and the dominant pneumococcic agent of pneumonia. As noted in other clinics, this organism attacked particularly infants and young children. Of the 104 patients with pneumonia from whom it was obtained, 79 per cent were in the first 3 years of life.

An attempt was made to evaluate the etiologic significance of Pneumococcus type XIV for each of the 104 patients in whom this organism occurred. In 62 per cent of the cases it was the only organism of importance isolated. Among the 40 patients with associated pathogenic organisms, Pneumococcus type XIV was apparently causative in 20 cases and a participating invader in 3 others. For 12 patients the relative etiologic importance of the organisms present could not be established, and in only 5 cases did associated organisms appear to predominate.

From late March 1938 to January 1939 potent concentrated type XIV rabbit serum was administered to 34 patients with pneumonia, of whom 22 were infants under 2 years of age and 29 were in the first 3 years of life. The average duration of acute febrile illness at the time of the first injection of serum was slightly less than three and a half days. Of 12 patients with pneumonia who did not receive serum during this period, 7 were children over 2 years of age; 8 entered late in the course of their disease or were recovering, 1 had mixed infection and a pulmonary abscess, 2 were treated with sulfapyridine and a mildly ill child was

asthmatic. To all 34 patients receiving specific concentrated serum, the serum, usually diluted in 5 or 10 volumes of a physiologic solution of sodium chloride, was given intravenously, only 1 infant receiving a small additional injection intramuscularly. The schedule of treatment was to give an initial dose of 0.5 to 1 cc. of serum, followed after two hour intervals by injections of 4.5 to 10 cc., provided no reactions had supervened. Four immediate and nine delayed reactions to administration of serum occurred in 13 patients, but only one reaction of each type was severe.

Of the 34 patients treated, for 31 the use of concentrated type XIV antipneumococcus serum appeared to be of benefit, 26 responding within thirty-six hours and 24 by prompt crisis within sixteen hours of the first injection. For 26 patients who received not more than two injections, a total of 7.1 cc. and plus or minus 30,000 units of antibody was the average dose requirement. Including 5 patients who received larger amounts of serum in three or more injections, the average dose for all patients benefited was 8.9 cc. and plus or minus 36,000 units. Failure to improve after administration of serum was accounted for in the 3 remaining cases by the presence of other types of pneumococci and purulent complications.

In the group of patients receiving serum, the average duration of acute febrile illness was five and fifteen-hundredths days as compared with ten and sixty-one hundredths days in the surviving patients not treated with serum. None of the 34 patients who received concentrated serum died, whereas among 55 patients not treated with serum before March 1938 the case fatality rate was 20.58 per cent for 34 infants under 2 years of age and 9.52 per cent for 21 children from 2 to 12 years.

Although the number of serum-treated patients is small, the clinical results indicate that for type XIV pneumonia in infants and children concentrated type-specific rabbit serum in relatively small doses has definite therapeutic value.

DISCUSSION

Dr. James D. Trask, New Haven: Has the method been successful in treating empyema?

Dr. Charles Hendee Smith, New York: For the last few months I have been enjoying a quiet joke with myself. For some twenty-odd years I have been going up and down the land saying that infants and children do have lobar pneumonia, and I have seen the pitying glance and the shaken head and heard the mutter, "The man is quite mad; they all have bronchopneumonia." Now sulfapyridine comes along, and my most severe critics are all reporting large series of cases of lobar pneumonia in infants. The point was proved by autopsies many years ago, and now it is beginning to be believed.

The use of type XIV serum has passed through four periods. The first began as soon as the types were discovered, with employment of horse serum, which was highly effectual. Dr. Nemir reported the results in two papers. Then the Department of Health stopped making type XIV serum, since they could not titrate it. I am told by the Lederle Laboratories, Inc., and the Department of Health that the type XIV pneumococcus will not kill laboratory animals and therefore is difficult to titrate. For this reason there was a good deal of difficulty in persuading Lederle to start making type XIV serum.

After the use of horse serum there was for a period no serum. That was a good control period because it showed that type XIV pneumonia is severe and has a long duration. It occurs mostly in young infants and has a high mortality.

When physicians began to obtain rabbit serum, they had excellent results again. Finally it was discovered that sulfapyridine apparently cures type XIV pneumonia as quickly as the other types. For the better part of the past winter it worked well, but recently there has been a wave of rather more severe type XIV pneumonia, and the patients have not responded quite as quickly. Probably the serum as well as sulfapyridine will have a place in treatment of this severe type of pneumonia in young infants.

DR. CLIFFORD G. GRULEE, Evanston, Ill.: I have long had a suspicion that there was something unusual in the West; I am sure that if Dr. Smith had come to the West some years ago, he would have found that lobar pneumonia in infants was diagnosed in a good many cases.

DR. EDWARD C. CURNEN JR., Boston: I am unable to answer Dr. Trask's question as to the effectiveness of specific serum in the treatment of empyema, as our experience has been too limited to justify conclusions.

INCIDENCE OF TYPES AND THERAPEUTIC RESULTS IN CASES OF PNEUMONIA OF INFANCY AND CHILDHOOD IN DETROIT. DR. BENJAMIN W. CAREY (by invitation) and DR. THOMAS B. COOLEY, Detroit.

This is a preliminary report on between 500 and 600 cases of pneumonia studied at the Children's Hospital of Michigan since December 1. Typing for the pneumococcus was done by the deep pharyngeal swab and culture method. When no pneumococci were found, search for other organisms was carried out. One of the difficulties encountered was the finding of more than one type of the pneumococcus in the throats of a considerable number of the patients. The ten most common types, in the order of incidence, were XIX, XIV, I, VI, XVIII, XVI, XV, XXIII, IV and VII. Types XIX and XIV were the most common in patients under 2 years of age, and type I was most common in patients over 2 years. The hemolytic streptococcus was found in 4 per cent of the cases and the staphylococcus in 1 per cent.

The cases were divided into three groups: In one the patients were treated with type-specific rabbit serum and in another with sulfapyridine, while in a third there was no specific treatment. Into this last group fell a number of cases in which the patients came to the hospital late in the course of the disease and a few cases in which death occurred within twenty-four hours of admission. In order to obtain comparable groups, all patients were excluded from the statistical analysis who died within twenty-four hours, who received no treatment until after the fifth day of the disease or who were admitted to the hospital after the fifth day of the disease.

The total fatality rate of all untreated patients, of all ages with pneumococcic pneumonia was approximately 12 per cent, of patients under 2 years 14 per cent and of those over 2 years 5 per cent. The fatality rate of the group treated with rabbit serum was 5 per cent and of the group treated with sulfapyridine 4 per cent.

With the exclusions mentioned, the fatality rate was 9 per cent for the untreated patients and 2 per cent for both the serum-treated and the sulfapyridine-treated group. The average duration of the disease was ten days for the untreated group and five days for each of the others.

A definite decrease in complications such as meningitis, otitis and mastoiditis was noted in the treated groups. The fatality rate of the untreated patients was remarkably low as compared with other years, indicating that the prevalent infection was unusually mild.

The group of patients with streptococcic pneumonia had a fatality rate of 28 per cent; all patients who died were under 2 years of age.

All of the patients with staphylococcic pneumonia died.

When treatment with sulfapyridine was started before the fifth day of the disease, it was noted that the average duration of pneumonia after the beginning of treatment was two days for patients whose blood level of free sulfapyridine was below 8 mg. per hundred cubic centimeters as compared with one day for those whose level was above 8 mg. When treatment was started after the fifth day of the disease, the average duration of pneumonia after beginning of treatment was four days for patients whose level was below 8 mg. as compared with two days for those whose level was above 8 mg. Considerable irregularity in absorption of the drug was observed. Patients of the same weight receiving the same dose showed widely different concentrations in the blood.

Toxic effects of sulfapyridine were rare and trivial. Cyanosis was noted in less than 10 per cent of the cases. Vomiting was the most troublesome symptom, but it seldom necessitated complete withdrawal of the drug. There were no cases of hemolytic anemia, leukopenia or hematuria. In the last six weeks of the study routine determinations were made of total hemoglobin, methemoglobin, sulfhemoglobin and oxyhemoglobin. Appreciable amounts of methemoglobin were occasionally observed, but sulfhemoglobin was never found.

DISCUSSION

DR. CHARLES HENDEE SMITH, New York: We physicians at Bellevue Hospital have treated only 90 patients, and so we have just begun. There was an unusually small incidence of pneumonia this winter.

I offer as a contribution the results of short time treatments. In most of the reported series and in the few cases for which Dr. Carey showed charts sulfapyridine was continued for several days after defervescence. In our series we started very early to try shorter treatment. In the cases so far analyzed, 10 per cent of the patients were treated only one day, 50 per cent two days and 20 per cent three days. Thus about 75 to 80 per cent of the patients were treated less than three days, and the results are just as good, with prompt crises and no complications.

There were a few deaths in cases of severe involvement, but we have not seen the relapses which have been dreaded by every one, fear of which made most writers administer the drug for a long time.

Our doses have been the same, 0.2 Gm. per kilogram the first day and 0.1 Gm. for the next day or two. Only a few patients were treated as long as five days. On account of the short period of administration, there were practically no toxic symptoms. There has been occasional vomiting. I believe that if the sulfapyridine is given after food or with food, for instance mixed with cereal or applesauce, the incidence of vomiting will fall off a good deal. In most hospitals drugs are administered to the patients at the convenience of nurses. Whether they are given after food or on an empty stomach should make a good deal of difference in the vomiting, as it does with almost every other drug. In scientific hospitals physicians sometimes forget the simple rule that most medicines should be given after meals.

As to Dr. Gerstenberger's remark that this drug should not be made generally available to the public, I believe the public is going to get it up to the limit. Every child who has a fever will be given sulfanilamide or sulfapyridine, in all probability. Physicians need warning that the latter need not be given for nine or ten days. If they believe that it must be continued for a long time after defervescence lest relapse occur, there will be a good deal of damage to kidney and liver blood.

Although most pneumonia observed in private practice is lobar, there is such a disease as bronchopneumonia. In about 5 per cent of our cases this winter the type was true bronchopneumonia, according to rigid tests; in those cases sulfapyridine apparently had little or no effect. If it is a virus disease, as I believe, this result may be perhaps expected. I refer those who think that bronchopneumonia is a pneumococcic or streptococic disease to the papers of McCordock and Muchenfuss, Siegfried and others. These show proved virus pneumonia in animals (dogs, swine, birds). The lung sections of these subjects are indistinguishable from those of infants with bronchopneumonia. I believe that bronchopneumonia, with its bizarre bacteriology, may well be a virus disease, and I hope somebody will prove or disprove this theory.

DR. BÉLA SCHICK, New York: Dr. Karelitz demonstrated the good results obtained by short treatment with sulfapyridine. My co-workers and I tried this form of treatment in about 80 cases; to our great satisfaction, the results of twenty-four or forty-eight hour doses of sulfapyridine were just as good as with the longer treatment. Not all patients will respond in this way, but it is certainly not necessary to give sulfapyridine for a long time in all cases.

Dr. Karelitz gave at first only one dose in twenty-four hours. We gave 0.2 Gm. per kilogram in the first twenty-four hours in three or four doses. We had 3 patients with positive blood cultures, and they reacted just as well as the others. I think it is important to continue this short treatment with sulfapyridine because it will, as Dr. Hendee Smith says, mean great progress.

Dr. James D. Trask, New Haven, Conn.: Often the etiologic diagnosis of pneumonia can be made by examination of nasal swabs. In pneumonia the pathogens appear in the nasal passages, and frequently one can recover the causative agent from the nose.

Dr. Charles G. Kerley, New York: I have observed so many epidemics of infection of the upper respiratory tract with pneumonia or other diseases that I have missed my count; but certain impressions have been made, and one is that these various epidemics, as they visit different sections of the country, are variable not only in their severity but in their association with other types of infection. For example, there are epidemics in which a large percentage of patients have aural complications, such as acute otitis and mastoid disease.

The epidemic of this year has been singularly free from aural complications. If there is anything that characterizes influenza as I have seen it from year to year, it is the variability in the type of the predominant associated infection.

I feel that sulfapyridine is a valuable remedy and that it will find its place. One cannot, however, evaluate any drug by one year's observation of an ailment as variable in its manifestations as influenzal pneumonia in children.

Dr. George M. Lyon, Huntington, W. Va.: Dr. Carey's slides indicate that even before the administration of sulfapyridine the leukocyte counts were low. Was this characteristic of the epidemic? Is it not of interest that such low counts occurred during true pneumonia? During the past two years my associates and I have with noteworthy frequency seen cases of apparently true pneumonia with no severe clinical manifestations but with characteristic roentgen shadows of the primary pneumonia type and yet with clinical courses of only twenty-four to seventy-two hours' duration. In these cases recovery occurred quickly without the administration of sulfanilamide, sulfapyridine or serum. Invariably the leukocyte count throughout the clinical course was only 6,000 to 10,000. Pneumonia of this type would have offered poor test material for the efficacy of sulfapyridine. I have felt that in some of these cases at least the diagnosis was uncomplicated influenzal pneumonitis.

Dr. Samuel Z. Levine, New York: It might be interesting to compare the incidence of types of pneumococci obtained by nose and throat swabs in New York with those reported for Detroit. Dr. Dooley has typed the organisms from the last 400 patients with pneumonia admitted to a hospital and has found precisely the same incidence as was found in Detroit. The most frequent types were I, VI, XIV, XIX and XXIII. In infants under 2 years of age types XIV, XIX and XXIII were predominant and in children over 2 years of age I, VI and XIX. It is assumed, of course, that the type obtained by pharyngeal and nasal swabs actually represented the offending organism.

It must be emphasized that a large number of typings performed in this way may show two, three, four and sometimes as many as six different types of pneumococcus simultaneously. In the absence of positive pleural or blood cultures, it seems rather difficult to say which, if any, organism found in the nose and throat was responsible for the pulmonary infection.

Dr. L. Emmett Holt Jr., Baltimore: I should like to ask Dr. Carey about the levels of sulfapyridine in the blood in his cases of staphylococcic pneumonia.

Dr. Thomas B. Cooley, Detroit: My name is on the program in connection with Dr. Carey's paper, but my function really was just to stand around and collect impressions while Dr. Carey did the work. Perhaps the most striking observation concerned the great differences in secondary pneumonia (the common type) in our infant wards this winter as compared with previous winters. There

was a change not only in mortality, which was striking enough, but in the duration and termination of the disease. That little babies, patient after patient, had a prompt crisis after a day or so of administration of the drug, as compared with the long-drawn-out and dubious course as we used to see it, was perhaps my most striking observation this winter, and it was the rule rather than the exception.

I should like to say something about Dr. Gerstenberger's impression, which seems to be rather common: that a good many of the patients did not get well so promptly as one might expect, considering the drop in temperature. After all they did get well; 2 or 3 per cent died instead of 15 or 16 per cent, and even if they didn't get well quite so soon as we thought they would when we saw the temperature drop, the fact that they got well after all was the important point, and the difference was only a day or so. Recovery was pretty prompt.

The general experience with untreated pneumonia this winter is rather important. We noted that the fatality rate for babies was much less than in most winters. The type of pneumonia was mild and I judge that has been true over the eastern part of the country, at least. That leaves the question open as to whether sulfapyridine will have such a remarkable effect when pneumonia is more severe or whether perhaps there will be an even greater difference between the mortality of treated and that of untreated patients. We do not and will not know until we have seen the drug used through a severe epidemic. I have a definite impression that in such an epidemic not only should serum and sulfapyridine be compared, but it should be ascertained how much more can be accomplished by the combined use of the two drugs, in at least a selected group of cases.

My impression in regard to empyema is a little different from that of Dr. Carey, who said he did not see that use of the drug made any difference. I do not know that it affected the development of empyema. It is hard to say whether the condition began before or after the specific treatment, but in watching the cases I gathered an impression that empyema did not progress so far.

We saw a number of patients in whom thick pus did not develop when they received this specific treatment, more than I suppose would have been possible without either the serum or the specific drug.

I cannot answer the question about the level of the drug in the blood of patients with staphylococcic pneumonia.

DR. BENJAMIN W. CAREY JR., Detroit: The levels of the drug in the blood of the patients with staphylococcic pneumonia were all high. In the first case the levels were about 15 to 19 mg. per hundred cubic centimeters, and with this range empyema developed and death followed. We purposely gave the rest of the patients with staphylococcic infection a higher dose than the other patients; their levels varied between 12 and 18 mg.

In regard to the leukocyte count, in many cases it was 5,000 to 8,000 when the patients were first admitted to the hospital, on the third to fifth day of the disease.

As to diagnosing the type of pneumonia by the organism found in the throat swab, you saw the number of cases in which we obtained more than one type of Pneumococcus and were unable to decide which was causative. We also have been conducting a study parallel with this investigation of pneumonia. This winter we picked out an infant ward that was crowded and cultured material taken from the patients' throats on the day of admission for Pneumococcus and for Streptococcus haemolyticus. Numbers of infants had pneumonia on admission and many others neither had pneumonia nor contracted the disease. For those who were in the hospital over a week we repeated cultures at weekly intervals.

I have not analyzed them completely, but there are several outstanding observations. For instance, the hemolytic streptococcus and the pneumococcus were not frequently found together in infants without pneumonia. In these patients the organisms were principally of types VI, XI, XV and XXIII. We may find other interesting data when we analyze this group of cases still further.

CLIFFORD G. GRULEE, M.D., *President*

Annual Meeting, Skytop, Pa., April 27-29, 1939

HUGH MCCULLOCH, M.D., *Secretary-Treasurer*

Second Session

Thursday Evening, April 27

EPIDEMIC DIARRHEA OF THE NEWBORN. DR. GEORGE M. LYON and DR. THOMAS G. FOLSOM (by invitation), Huntington, W. Va.

An epidemic of diarrhea of the newborn was observed in the nursery of a general hospital in August 1938. In December 1926 and October 1934 similar epidemics occurred in the same hospital. Except in size they were in all essential respects similar. Contemporaneously with each, acute epidemic influenza was prevalent within the community. We appreciate and deplore the carelessness with which this clinical term is generally used. Short of actually limiting its use to a condition in which there is either demonstration of the virus or microscopic evidence of invasion of tissues by the virus, we have made every possible effort to use it carefully. The present lack of exact methods for accurately diagnosing epidemic influenza prevents any one from speaking precisely about a clinical condition which is altogether too real and too important to be passed over lightly simply because there are no exact or easily applicable methods for proving or disproving its clinical presence. Epidemiologic characteristics, postmortem observations and clinical patterns similar to those of characteristically acceptable epidemics of influenza supplied ample, even if not absolute, evidence of the prevalence of this disease within the community during the three periods referred to.

An obstetric patient in labor was admitted to the hospital with fever and leukopenia. No attention was paid to the fact that she reported having had a "grippy" sickness the previous week. She was delivered by cesarean section. Her boy was placed in the general newborn nursery, which is not under pediatric supervision. Again without pediatric supervision, he was taken every four hours to her to nurse and then returned to the nursery, in spite of the fact that the mother required cough sedatives for her respiratory distress. He was normal the first five days. Then his temperature rose to 102 F.; he became hyperesthetic and cyanotic and presented symptoms of an intracranial accident. At this time the mucous membranes of his oropharynx were red and injected and his ear drums reddened. On the eighth day he had convulsions, several loose stools and a temperature of 103 F. He received 18 cc. of his father's blood intramuscularly for reduction of intracranial bleeding. He died on the tenth day. Neither diarrhea nor dehydration was apparently important as a cause of death. Permission for autopsy was not obtained.

Thirty-six hours after the onset in the first case, an infant in an adjoining crib presented similar symptoms; the child died within forty-eight hours. Then the epidemic burst forth explosively; the true condition became apparent, and the nursery and obstetric services were closed to new admissions.

Twenty-one newborn infants were exposed, 16 were affected and 5 died. Three of the most critically ill patients presented symptoms almost identical with those in the fatal cases, namely, temperatures over 105 F., prostration, convulsions, cyanosis and diarrhea of mild to moderate severity. Loss of fluid by vomiting or by bowel movement was not excessive. Fluid balance was readily maintained, and there was but little dehydration. The patients were not acidotic. Each of the 3 critically ill infants received intramuscularly 30 cc. of citrated whole blood from a patient recently convalescent from an apparently genuine attack of epidemic influenza. In each instance there was a remarkable improvement in a few hours. Temperatures returned nearly to normal, recoveries were uneventful, and although the patients were afebrile there was for approximately two weeks a tendency to

loose stools. A physiologic solution of sodium chloride was early given subcutaneously, and dextrose solution and whole cultured lactic acid milk were given by gavage. Diarrhea in the critically ill patients was not more severe than in those with only moderately severe involvement.

There is good reason to believe that in the three epidemics of diarrhea of the newborn described the condition was in reality a form of epidemic influenza or a closely related virus infection. The use of convalescent blood in the manner described is worthy of further trial.

DISCUSSION

DR. THOMAS G. FOLSOM, Huntington, W. Va.: It is realized that in this report we present a small number of cases and have no true prearranged controls. However, I believe the results Dr. Lyon obtained with convalescent influenza serum will seem significant to the most analytic.

Of the 8 babies who had high fever, respiratory difficulty, cyanosis and convulsions, those treated with convalescent influenza serum (3) lived and those not so treated (5) died.

The only severely ill patient under my care who recovered had a moderately high fever, respiratory difficulty and some cyanosis but no convulsions. This baby's illness was protracted over six weeks, during which he received two transfusions of whole blood.

The 5 fatal cases may be briefly reviewed:

Two deaths occurred before we realized that we were confronted with epidemic diarrhea of the newborn. The cause of death in the first case described in Dr. Lyon's paper was attributed to acute nephritis by the pediatrician who was in attendance. The renal changes were apparently just a sign of severe toxemia. This infant received 18 cc. of his father's blood intramuscularly. The second death I attributed to cerebral hemorrhage because of respiratory difficulty, cyanosis, convulsions and some blood in the spinal fluid, although the baby was 7 days old at the time. The next 2 babies to die were treated vigorously for four and five days, respectively. The first received two transfusions of whole blood and the second two transfusions of citrated blood.

The fifth to die was a premature twin, who lived only a few hours after the onset of his illness.

Autopsies were done in the last 3 cases. To me the outstanding change, which I believe was the immediate cause of death, was the marked cerebral edema and congestion; this could easily explain the signs and symptoms of cerebral hemorrhage, including bloody spinal fluid.

In 5 other cases that were encountered the condition was classified as mild, principally because the patients had no high fever, convulsions, respiratory difficulty or cyanosis and required little special treatment, although diarrhea had begun and from 3 to 12 ounces (85 to 340 Gm.) had been lost in twenty-four hours. These babies were fortunate in having an adequate supply of breast milk; they were given infusions and sent home with a prayer.

I am not prepared to say whether removal from the hospital played any part in the favorable outcome.

DR. BENJAMIN KRAMER, Brooklyn: In 1935 there was an epidemic of this type of diarrhea of the newborn at the hospital with which I am connected. There has been none since. Dr. Zuger, then the resident, made an epidemiologic study to see if he could trace the origin of the epidemic and its mode of spread.

He found that it originated with 2 babies whose mothers occupied one room. These babies infected other babies in the nursery. Subsequently an infected newborn child who was not ill was transferred through mistake to a clean nursery. This baby subsequently contracted the disease, and this instance of infection was followed by others in the same nursery. About 6 per cent of the newborn babies had the disease.

The closing of the nursery and of the adjoining maternal ward and complete renovation of both with complete change of nursing personnel failed to check the epidemic, which stopped only when the entire maternity building and all nurseries were closed.

Sick infants were transferred to the pediatric ward, but although in that ward there were some infants as well as older children at no time was there any cross infection.

From the chemical point of view these patients showed the most profound degree of acidosis I have ever seen in infants. The carbon dioxide-combining power of the blood plasma in many instances was as low as 10 volumes per cent and in some cases even less. This appeared to be due to a high chloride concentration.

The treatment consisted of starvation, continuous venoclysis with a physiologic solution of sodium chloride and 5 per cent dextrose and gradual restoration to an adequate diet.

The mortality was between 40 and 60 per cent.

Dr. Joseph Brennemann, Chicago: These epidemics of the newborn have a somewhat different interest and significance to those who have practiced pediatrics for a long time than they have to the younger men. Until a few years ago I had never encountered or heard of the type of epidemic diarrhea there has been in recent years. Apparently every large city is having epidemics of this sort in the maternity wards. The condition in these cases does not in any way impress me as being like the ordinary summer complaint that used to be so prevalent. To me it is something new; possibly Dr. Lyon's paper gives some clue as to the cause.

Most infections, of course, enter the body through the respiratory tract, and I have never felt that this epidemic disease was essentially diarrhea—in other words, I believe that the diarrhea was merely a part of some other infection. I have for years believed that the newborn infant is relatively immune to disease, except such a condition as impetigo. I once talked with Dr. Finkelstein about it, and he expressed exactly the same idea—that up to the third month there is noticeable immunity as compared with the succeeding period. For this reason, among others, I feel that these epidemics are based on a new and unique cause.

Furthermore, I have yet to be convinced that the elaborate prophylactic measures advocated will prevent further outbreaks of this sort, at least in the initial stages.

Dr. George M. Lyon, Huntington, W. Va.: One of the main reasons for bringing this paper before this group was to emphasize a tremendously important problem arising in the nursery for the newborn in a general hospital in a small town. The control of communicable disease therein presents a real challenge to the pediatrician's ability and persistence.

In the instance described an obstetric patient, without control or check as to her freedom from contagion, was admitted to the obstetric service of a general hospital. At the same time other patients were entering this service to be delivered with the idea that in that hospital they and their infants would be protected from the spread of contagious diseases. Technics better than those existing at present must be evolved and utilized.

Like Dr. Brennemann, I do not know about the effectiveness of prophylactic measures. It is interesting, however, that 1 of the 3 newborn infants receiving convalescent whole blood left the hospital on the fourth day after delivery and did not show any signs of trouble until the eighth day.

In answer to Dr. Kramer, there was little in the behavior of these infants to indicate acidosis. As was stated, dehydration was not at all remarkable. This is a point of considerable significance. With Dr. Kramer I have seen many infants with acidosis, and I think we understand each other's ideas on the subject. These newborn infants did not die of acidosis any more than do older children with Shiga bacillus dysentery who die before a loose stool is passed. In fact, their clinical behavior was similar.

The gains in weight which occurred during the first week merely indicate that the infants were not physiologically subnormal at the start and that they were gaining well at the onset of illness. None of the local pediatricians was responsible for the admittedly too rapid gains in weight during the first week. Pediatricians

were not consulted until the babies were in trouble. While we agree with Dr. Smith that the gain was certainly too rapid, we cannot agree with him that it was cause of the epidemic diarrhea. The "stuffing" of newborn babies during their first two weeks of life should be discouraged. Although it increases neonatal illness appreciably, it is not the cause of epidemic diarrhea of the newborn.

The impression we obtained from our contact and experience with this epidemic was that the disease was really a generalized infection which was particularly damaging to the brain and to the gastrointestinal tract and that the diarrhea was just part of a generalized infection rather than a primary bacterial invasion of the intestinal tract, as has been so frequently intimated in the literature. There is good reason to believe that the epidemic diarrhea of the newborn we have observed has in reality been the clinical expression of epidemic influenza in susceptible newborn infants, particularly when it is favored by the practice of crowding newborn babies in the nurseries of general hospitals, which is so common today.

INCIDENCE OF DYSENTERY IN GASTROENTERITIS. DR. MERLIN L. COOPER (by invitation), DR. GLENN E. CULLEN, DR. M. L. FURCOLOW (by invitation), DR. ESTELLE W. BROWN (by invitation), and DR. A. GRAEME MITCHELL, Cincinnati.

A study was made of 209 infants and children suffering from acute diarrhea during the summer of 1938 in Cincinnati. Stools were obtained within thirty minutes of the time they were passed. From 745 stools of these 209 patients cultures were made on 11,530 plates. The bacteriologic study was extensive. The incidence of dysentery in this group was 49 per cent. The fatality rate for the two groups of patients was not significantly different, being 12.7 per cent for those with dysentery and 15.9 per cent for those without dysentery. The two groups followed the same pattern of seasonal incidence. The duration of symptoms in the two groups was approximately the same. Acute diarrhea in early infancy was usually not due to dysentery bacilli, but in three quarters of the cases of patients over 1 year of age the condition was due to dysentery. Duration of the symptoms at the time of stool culture was approximately the same in both groups. The organisms found were of the Sonne, the Flexner and the Oxford V X type and dulcitol fermenters. Desoxycholate-citrate medium was far superior to Endo's medium, eosin–methylene blue medium and MacConkey's medium. Desoxycholate citrate, however, was relatively inefficient, since it gave only 58 per cent positive results on 920 plates of 46 patients known to have dysentery. Endo's medium gave only 28 per cent positive results on 920 plates of the 46 patients with known dysentery. It is suggested that any report of the incidence of dysentery in a given community or epidemic which has relied on examinations of the stools with Endo's medium alone should be reevaluated on the basis of these findings.

DISCUSSION

DR. HENRY J. GERSTENBERGER, Cleveland: Did Dr. Mitchell find a difference in the pathologic picture between the two groups of children on whom autopsy was performed? Were the lesions in the intestines the same, or did not one group have lesions principally in the large intestine and the other group in the small intestine?

DR. A. GRAEME MITCHELL, Cincinnati: Some of the patients with dysentery showed little change at necropsy, with no more ileocolitis than those we had considered, by nature of the study, not to have dysentery. Many of the patients with dysentery died rather soon, and perhaps there was not sufficient time for ileocolitis to develop. But I think our general opinion has been, at this time and previously, that not only clinically but sometimes pathologically it is difficult to distinguish these two groups of patients in the early stages of gastroenteritis.

STUDIES OF VITAMIN A. DR. HUGH W. JOSEPHS, Baltimore.

A series of observations on children showed that there is a correlation between the vitamin A and the carotene content and the cholesterol and the total lipid

content of the blood serum. This is not unsuspected when the fat solubility of vitamin A and carotene is borne in mind, but in the literature it has not been considered in interpretation of the variations of these substances in the blood serum or in explanation of such correlations as that between vitamin A or carotene and cholesterol. It is considered probable that vitamin A circulates in solution in the blood fat. Its concentration in the blood fat may have to be considered before a conclusion is reached in regard to deficiency or in regard to the ease with which vitamin A can be distributed to the tissues.

DISCUSSION

DR. SAMUEL W. CLAUSEN, Rochester, N. Y.: Dr. Josephs pointed out an important relationship that apparently most physicians have missed. I am wondering whether he studied the effect on the vitamin A content of the plasma due to any factor which may cause lipemia other than alimentary lipemia, such as white snake root poison or narcosis. The storage of vitamin A in the liver seems to be controlled by conditions which are little understood. Still less is known of the factors which control liberation of the vitamin from the liver.

DR. A. F. ABT, Chicago: What method does Dr. Josephs use to determine the vitamin A in the blood?

DR. HUGH W. JOSEPHS, Baltimore: In answer to Dr. Clausen's questions, I have not studied specifically anything except the effect of ingestion of fat. This was unsuccessful in mobilizing vitamin A from the liver. It may be that in these experiments the blood fat was not sufficiently raised to give a final answer to the question.

In regard to narcosis, it was studied in France several years ago by Chevalier. He found that there was liberation of vitamin A from the liver into the blood.

The method used was that sent me by Dr. Clausen two years ago. I do not know whether his report has been published yet, but the method used the antimony trichloride reaction. In one or two points it varied from Dr. Clausen's procedure. The comparison was made not in a colorimeter but with tubes of copper sulfate arranged in a series from 10 per cent down to about 0.625 per cent, at which barely visible blue color could be recognized. This year we have been determining the vitamin A by the photoelectric colorimeter; the two methods check rather closely at medium levels but not at high or low levels.

VITAMIN D INTOXICATION IN INFANCY. DR. S. G. ROSS and DR. W. E. WILLIAMS (by invitation), Montreal, Canada.

Four cases of hypervitaminosis D with 2 recoveries and 2 deaths are reported. Permission for 1 autopsy was obtained. Ages ranged from 8 to 14 months. The vitamin had been administered over several months as viosterol in doses of 20,000 to 40,000 U. S. P. units daily. The symptoms in all cases were anorexia, loss of weight and vomiting.

The first patient was admitted for pyelonephritis. The findings were malnutrition, weakness, muscular hypotonia, peripheral facial palsy and anemia. The urine showed albumin, pus and casts. Chemical examination of the blood showed increased nonprotein nitrogen, hypercholesteremia, 18 mg. of serum calcium per hundred cubic centimeters and 5.1 mg. of inorganic phosphorus. Roentgenograms of long bones showed increased density at the zone of provisional calcification. Proximal to this was a zone of rarefaction and proximal to this a zone of increased density. The zone of rarefaction increased in width during the stay in the hospital. There was generalized periosteal thickening in most of the bones of the body, with a dense outer layer and a rarefied area between this and the dense bone. Urinary excretion of calcium increased even with a low calcium diet. Administration of vitamin D was stopped, and this was followed by gradual improvement. The serum calcium level gradually dropped to normal; the urine cleared, and a year later roentgenograms showed normal bones.

The condition in the second case was similar to but milder than that in the first. Hypercalcemia was present. The kidneys were not affected, and the long bones showed merely increased density in the zone of provisional calcification. Recovery was rapid, and after several months hypercalcemia had disappeared.

The last 2 patients were premature twins. One was admitted to the hospital with bronchopneumonia, anemia and albuminuria. Roentgenograms showed increased density at the zone of provisional calcification, with an area of rarefaction proximal to this. The long bones showed periosteal thickening, with a dense outer layer and a rarefied inner zone. This patient died, and permission for autopsy was not obtained. His twin brother had died suddenly a few days before, during the course of pneumonia. Autopsy showed asphyxia from aspiration of mucus and food into the trachea. Bronchopneumonia was also present. Histologic examination showed extensive metastatic calcification. There was generalized deposition of calcium in the arteries, in the inner layer of the media. There was also calcification in the cardiac muscle. The kidneys showed calcification, especially in the tubules. Calcification was also present in the lining of the alveoli of the lungs and in the bronchi. The stomach showed deposition of calcium in the muscularis mucosa as well as in the basal portion of the cells comprising the mucosa. The bones were not examined.

These cases illustrate the nutritional and metabolic disturbances caused by this condition and the pathologic picture at autopsy. They serve as a warning against overdosage with this powerful agent.

DISCUSSION

Dr. Donovan J. McCune, New York: What evidence has Dr. Ross relating to renal function both during the period of intoxication and during recovery? Was the toxic effect related to the type of preparation of vitamin D he used?

Dr. S. Graham Ross, Montreal, Canada: In the first case the child showed evidence of renal damage, with albumin, casts and white blood cells in the urine. After four months the albumin, casts and white blood cells had entirely disappeared from the urine, and the child showed no clinical evidence of renal disease of the kidneys. In the second case there was at no time any evidence of renal disease. In the third case there was albuminuria on admission.

As to the question of toxisterol's being present, the preparation of viosterol that has been used is produced under a license from the Steenbock Foundation and has been widely employed locally for some time. I have not had it examined for toxicity but feel that this possibility must be ruled out. Another possible explanation is that these infants were peculiarly sensitive to excessive doses of vitamin D in the form used.

Determination of Ascorbic Acid. Dr. Allan M. Butler and Dr. M. Cushman (by invitation), Boston.

The validity of the commonly used methods for the determination of the ascorbic acid in whole blood has been studied. The data in the literature give the concentrations of ascorbic acid in red blood cells as greater than, equal to, or less than that in the plasma. Moreover, there is a difference of opinion as to whether analyses of whole blood or of plasma give more reliable information concerning vitamin C deficiency or saturation.

The commonly used titrimetric method of analyzing whole blood by means of the indicator dyes 2, 6-dichlorophenolindophenol and methylene blue was adapted to colorimetric photoelectric determination according to the methods of Meunier, Mindlin and Butler; Maughan, Evelyn and Browne, and Bessey. In this manner the rate of reduction was visualized, and the rapid reduction characteristic of ascorbic acid could be distinguished from reduction proceeding at a slower rate. The analytic data suggest the following conclusions:

1. There are satisfactory methods for the determination of ascorbic acid in plasma or serum.

2. Precipitation of whole blood with trichloroacetic acid or metaphosphoric acid in room air results in the oxidation of ascorbic acid and the possibility of gross error.

3. The filtrates of whole blood obtained by the method of Emmerie and Van Eekelen, in which mercuric acetate is used as a precipitant and hydrogen sulfide as a reducing agent, contain substances other than ascorbic acid which reduce 2, 6-dichlorophenolindophenol. Moreover, the use of trichloroacetic acid in this method may cause a loss of ascorbic acid.

4. White blood cells contain a substance which in the methods of analysis used in this study reduces 2, 6-dichlorophenolindophenol and methylene blue as in the reduction due to ascorbic acid. In the normal person the ascorbic acid or apparent ascorbic acid concentration of white blood cells averages 25 mg. per hundred cubic centimeters. Thus the white blood cells account for approximately 20 per cent of the ascorbic acid concentration of the average whole blood. The concentration in white cells may reach as much as 100 mg. per hundred cubic centimeters of white blood cells. This means that in the presence of leukocytosis the white blood cells may be the major factor in determining the concentration of ascorbic acid in whole blood.

These conclusions indicate that at present there is no chemical method of determining the concentration of ascorbic acid in whole blood or in the majority of tissues the validity of which has been adequately demonstrated.

PHOSPHATE SOLUTIONS IN THE TREATMENT OF INFANTILE RICKETS. DR. HENRY J. GERSTENBERGER, Cleveland.

On the basis of the work which was reported at the 1938 meeting of this society and which showed that phosphate and not calcium solutions were able to bring about the healing of the long bones of monkeys ill with low phosphorus rickets, as judged by the roentgenograms and by the return of the blood serum level of phosphorus to normal, rachitic infants were given phosphate solutions, either orally or parenterally.

The study concerned 4 infants, 2 boys and 2 girls, who were ill with low phosphorus rickets. After observing the patients sufficiently long to be certain that no so-called spontaneous healing had taken place—a precaution little applied generally and yet absolutely essential to a dependable, scientific investigation—the 2 girls were given phosphate solutions by the oral route and the 2 boys by the parenteral route. The former showed no signs of healing in the roentgenograms or in the blood. One of these patients was treated for nine weeks and received a dose 50 per cent greater than that given the other patient; notwithstanding, there was no significant change in the level of the serum phosphorus, which at the beginning of the treatment was 1.4 mg. per hundred cubic centimeters and at the end 1.7 mg.; the calcium levels were, for these two periods, 9.8 and 10.3 mg., respectively.

The 2 boys, who were given the phosphate solutions parenterally, responded with signs of healing both in the roentgenograms and in the blood. One of these 2 patients, however, because of a tendency to development of latent tetany, could be given but half of the desired dose; as a result, the healing changes in the roentgenograms were irregular and not marked. For the other boy, however, there was registered in the roentgenograms a complete phosphatization (calcification) of the distal end of the radius and a nearly complete result in the distal end of the ulna. At the beginning of the treatment, the blood serum level for the calcium was 10.1 mg. and for the phosphorus 2.6 mg.; at the end of the treatment, after forty-two days, the calcium level was 9.6 mg. and the phosphorus 4 mg. Because of the altered disposition of the infant the study was terminated before absolutely normal conditions were revealed in the roentgenograms and in the blood.

It is evident from the results just described that the phosphate solutions orally administered to the girls produced absolutely negative therapeutic results, whereas the effects of the phosphate solutions parenterally administered to the boys were highly positive.

Even though these findings strongly suggest that hindered absorption, rather than decreased retention, is responsible for the hypophosphatemia of infantile rickets, I do not feel justified at this time in unqualifiedly accepting this conclusion.

NUTRITIONAL REQUIREMENTS IN INANITION. DR. L. EMMETT HOLT JR. and CHARLOTTE N. KAJDI (by invitation), Baltimore.

The problem of inanition possesses a clinical interest, for inanition is an important contributory cause of death with many gastrointestinal disorders. The essential food requirements of a starved organism are not necessarily the same as for growth or maintenance. The organism may possess adequate reserves of certain essentials, whereas others may quickly become exhausted. Moreover, it is possible that under such conditions of stress deficiencies may appear that have not hitherto been recognized. The experiments reported were designed to throw light on the food requirements in inanition by determining the ability of particular foods, given singly, to prolong the survival of starved rats. Data were obtained illustrating the effect on survival of a number of different proteins, carbohydrates, fats, minerals and vitamins. It was concluded that in the early weeks of starvation, at least, there is no evidence of deficiency of amino acids, minerals, fat-soluble vitamins, nicotinic acid or riboflavin. In sharp contrast to these results it was found that a deficiency of thiamin could be detected relatively early in starvation, particularly when the diet consisted of carbohydrate alone. Under these circumstances the addition of thiamin causes a striking prolongation of life.

Certain peculiarities were apparent in the behavior of animals given these diets of single foodstuffs. Among these were the differences in water consumption when fat, carbohydrate or protein food was given. With a pure fat diet relatively little water is required, and the small quantity ingested has little relation to the food intake. With a pure carbohydrate diet the water intake is fully twice as great as with a fat diet, and the water ingestion is closely parallel to the food intake. The water requirement is even greater with a pure protein diet, and here again a parallelism between food intake and water intake is striking. The suggestion is made that this water-sparing action of fats may be a factor of importance in conditions associated with scarcity of water.

DISCUSSION

DR. HUGH W. JOSEPHS, Baltimore: Is it possible that the yeast-contaminated maltose that Dr. Holt used supplied the vitamin B_1 factor that was missing in the rats and that that was perhaps why they did better with the impure maltose than with the pure?

DR. WILLIAM W. SWANSON, Chicago: Were the rats which were taking lactose and galactose also given mineral mixtures? It seems that since these rats took more water, they would have a greater output and might therefore lose more minerals than rats taking other carbohydrates.

DR. L. EMMETT HOLT JR., Baltimore: It is possible that Dr. Josephs' theory is correct. We made no observations on the vitamin B_1 content of the contaminating mold.

I shall have to answer Dr. Swanson's question in the negative. We have not studied the question of mineral deficiency in animals receiving lactose or galactose. Because of Dr. Mason's observations on idiopathic human galactosuria, which suggested that unutilized galactose may produce damage to the liver, we examined the liver of an animal or two who died from galactosuria but found a normal histologic picture.

Third Session

Friday Morning, April 28

SIMPLER METHODS FOR DETERMINING BASAL METABOLIC RATES OF CHILDREN. DR. HAROLD L. HIGGINS and DR. WALTER R. MACLAREN (by invitation), Boston.

Inaccuracy in the determination of the basal metabolic rates of children is referable not so much to the technical procedures as to the subject. The child must be in a basal state, or in a close approximation to it, for a sufficient length of time for measurements to be made. If the baby under 1 year old is given his milk, he readily falls asleep and offers little difficulty. The older child will usually cooperate and try to keep still; the child with a mental age over 8 years can usually adapt himself to the use of the mouth piece, and the chamber method is unnecessary. The child from 1 to 6 years old who will not sleep, cannot keep still or is easily frightened offers the big problem. A psychologic approach is frequently unsuccessful, and sedatives are probably undesirable. Much more hopeful is the obtaining of the test at night, when the child is naturally sleepy; if the test can be made simple enough to be performed at the bedside, a practical goal will be reached.

Two new technical procedures are being applied in our laboratory to increase the accuracy and to expedite the determination of the basal metabolic rate.

The amount of carbon dioxide (or oxygen deficit) in the air drawn from the chamber in a given time must be corrected for the different amounts of carbon dioxide (residual carbon dioxide) present in the chamber at the beginning and at the end of the period. It is often hard to determine this residual correction accurately. In a small box there is a small correction, but also there is difficulty in the removal of heat produced by the patient. In a large box, the effect of the correction may be counterbalanced by lengthening the period, but that means that the child must stay quiet a longer time.

In practice, air is drawn through the chamber at a constant rate. With the child at rest a practically constant volume of carbon dioxide is being eliminated into the box. The relation $\frac{CO_2 \text{ produced}}{\text{ventilation}}$ will thus be constant. If the volume of carbon dioxide in the chamber is higher (or lower) than this constant at the time the ventilation is started, it will gradually fall (or rise) along an exponential curve to approach the constant $\frac{CO_2 \text{ produced}}{\text{ventilation}}$. The formula for this curve follows; if the percentages of carbon dioxide in the air leaving the chamber on two occasions, a known time apart, are determined, the constant $\frac{CO_2 \text{ produced}}{\text{ventilation}}$ and thus the production of carbon dioxide may be calculated.

The formula is $a = y + \frac{y - b}{e^{\frac{rt}{v}} - 1}$

In this formula a = per centage of $CO_2 = \frac{CO_2 \text{ produced}}{\text{ventilation rate}}$, y represents the second determination of percentage of carbon dioxide leaving the chamber; b, the first determination of percentage of carbon dioxide leaving the chamber; e, 2.718 (natural logarithm); r, the ventilation rate (liters per minute); t, the time in minutes between the first and the second sampling of air leaving the chamber, and v, the volume of the chamber. If r and t are adjusted so that $\frac{rt}{e\ v}$ equals 2 or 1.5, the calculation is simple.

Accurate gas analysis for carbon dioxide, oxygen, or both is usually requisite for basal metabolic determinations for children, as gravimetric determinations of carbon dioxide require long test periods. The gas analysis by the Carpenter-

Haldane apparatus has been accurate for this purpose; it is time consuming, twenty minutes being necessary for a single determination. The apparatus must be kept in working order, and the technician must have had considerable experience. The colorimetric method of determining carbon dioxide described by Higgins and Marriott has been adapted for our use by a photoelectric cell colorimeter.

The air to be analyzed is passed through 18 cc. of a 0.001 normal solution of sodium bicarbonate containing 0.004 per cent phenolsulfonphthalein at a rate of about 200 cc. per minute; in less than forty-five seconds the solution will be saturated with carbon dioxide at the tension of that gas in the sample, giving a definite p_H and color to the sample.

The colorimetric reading on a galvanometer is compared with readings of 2 samples of known carbon dioxide content which are kept in gas cylinders under pressure. These known samples give check readings with each series of analyses and obviate the necessity of correction for variations in temperature, in barometric pressure and in the dye content of the solution.

The accuracy of the analysis is ten times that of the original method, or approximately 0.5 per cent of the total carbon dioxide (0.400 per cent $\pm$ 0.002).

The method allows for frequent analyses, or even constant readings, of the carbon dioxide leaving the metabolism chamber.

DISCUSSION

Dr. Fritz B. Talbot, Boston: The importance of any advance of this sort can be appreciated only by those who have done this work from the very beginning. When metabolism testing in a chamber was first undertaken, three months were spent in finding all the leaks in the chamber before one could start working. The age period during which it is most difficult to obtain accurate figures, of course, is that between 2 and 7 years. Any method that will shorten the test period is of great advantage. Children are often quiet for five, ten or even fifteen minutes; when it comes to a half hour or an hour period, they naturally get tired, and any method that will shorten the time should greatly increase the accuracy of the findings.

Of course, it should be emphasized that in work with these children of 2 to 7 years the accuracy of basal figures depends more on the status of the child, in many instances, than on the accuracy of the investigators, for trained investigators do not make mistakes in their measurements. When older children are considered the question is different.

There are only about four or five places where the metabolism of babies and young children can now be measured.

I want to emphasize the fact that after the figures have been obtained, plus or minus findings should not be accepted without a little use of the brains. A great many physiologic factors have to be taken into consideration in the interpretation of the figures.

Dr. Harold L. Higgins, Boston: The metabolism chamber does not need to be elaborate or absolutely air tight. The chamber is under slightly negative pressure, so if air leaks in it is essentially outdoor air and does not affect the determination or the results obtained.

A satisfactory chamber could be made, I think, for $50. It is necessary to watch for means of eliminating heat; in a metal chamber the heat can be got rid of, while in a wooden chamber it is hard to keep the temperature from rising.

With regard to the photoelectric colorimeter, we have one that was constructed by Dr. MacLaren; it cost about $75, considerably less than colorimeters on the market.

Influence of Cobalt on Iron Transportation in Blood. Drs. Katsuji Kato and Vivian Iob (by invitation), Chicago.

For the study of iron transportation in blood, experimental polycythemia in animals, produced by the simultaneous administration of iron and ammonium

citrates and cobaltous sulfate, was chosen. In animals previously made anemic by an exclusive milk diet, this combination of iron and cobalt produces a pronounced increase in red cell count, hemoglobin values and hematocrit readings (Kato, 1937). In normal animals the increase is never so marked. Two groups, comprising 6 rabbits and 3 dogs, were used. The rabbits were maintained on a stock diet adequate for normal growth. The dogs were fed liberal amounts of whole wheat bread soaked in 50 per cent evaporated milk into which iron and cobalt were incorporated. For all animals the daily dose of iron and ammonium citrates was 1 Gm. and that of cobaltous sulfate 0.1 Gm.

Quantitative chemical analyses were made of the three principal forms of iron in blood: total blood iron, total serum iron and dialyzable blood iron, after treatment with dilute acids. Oxygen capacity and acid hematin content were also determined. Complete hematologic and histologic studies were made at the same time.

The chemical study on the rabbits revealed that the total iron of the blood increased nearly 55 per cent above the control values after administration of cobalt. There was a comparable rise in hemoglobin, but the iron values calculated from the oxygen capacity of the blood were consistently lower than those obtained by actual analysis. The degree of discrepancy increased in parallel with the extent of the polycythemia. On the other hand, serum iron remained at a fairly constant level in both rabbits and dogs. In rabbits only was there an appreciable increase in the dialyzable iron.

The peripheral blood revealed a continuous rise in all values, including red cell count, hemoglobin volume and packed cell volume. The most striking feature was the tremendous increase in reticulocytes during the active stage of polycythemia.

From these observations it is inferred that the influence of cobalt in accelerating the production of erythrocytes and hemoglobin appears to be due to direct stimulation of the hemopoietic centers in the bone marrow. The metal may have a possible influence in transportation of iron by increasing slightly the amount of dialyzable iron in the blood. Serum iron values were not affected. The augmenting difference between iron values calculated from oxygen capacity and values obtained from direct determination points to a third type of nonhemoglobin iron, the form of which is as yet unknown.

DISCUSSION

DR. ALFRED H. WASHBURN, Denver: Did Dr. Kato have any reticulocyte counts or other evidence, aside from the number of red cells in the peripheral blood, showing that there was actually an increase in the rate of production of red cells?

DR. KATSUJI KATO, Chicago: I did not mention the other aspects of the study. I followed the reticulocyte count; during the peak of polycythemia there is a great increase in these young elements. I have also studied the tissues, particularly the bone marrow, liver and lymph nodes, and the only evidence I found of increased hemopoiesis was the marked hyperplasia of the myeloid tissues.

CONTINUOUS CALCIUM AND NITROGEN BALANCES BEFORE AND AFTER THE MENARCHE. DR. JOSEPH A. JOHNSTON, Detroit.

Continuous calcium and nitrogen balances, with concurrent determinations of basal metabolic rates, were recorded for a group of girls during the year of the menarche. The instability of the basal metabolism during this time, with a definite tendency to a premenarchial rise and a postmenarchial fall, was confirmed. A period of high retention of calcium and nitrogen was followed by a sharp fall and subsequent recovery; while in some instances the fall was closely related to the onset of the first menstrual period, it was sometimes delayed beyond this point and sometimes preceded it. Retentions were directly correlated with the basal metabolic rates, the higher retentions occurring with higher rates and vice versa. In records continued uninterruptedly over periods as long as three hundred

days, a striking tendency is evident for retentions to occur in cycles, but the length of these was variable and did not seem to be correlated with the menstrual cycle.

DISCUSSION

DR. PHILIP C. JEANS, Iowa City: How much, if any, vitamin D was used in relation to the calcium balance studies?

DR. JOSEPH A. JOHNSTON, Detroit: No particular provision was made for vitamin D. That point is being studied separately. In the case of 2 girls, two and three years, respectively, after the menarche, the addition of viosterol made no difference. Phosphorus values were not determined. Likewise, variations in intake between 900 and 1,400 mg. made no significant difference in retention. Lower levels of intake were not studied.

DR. CLIFFORD G. GRULEE, Evanston, Ill.: According to the latest ideas, pediatrics now concerns patients up to the age of 17 or 18 years.

LATE RICKETS WITH GLYCOSURIA AND ORGANIC ACID ACIDOSIS (FANCONI TYPE). DR. D. J. MCCUNE (by invitation), DR. H. H. MASON and DR. H. T. CLARKE (by invitation), New York.

An only child of consanguineous parents was recognized to have rickets in infancy. Despite irregular treatment with cod liver oil and sunlight the disease became progressively more incapacitating, and the boy was finally bedridden. At 9 years of age he was severely dwarfed and exhibited the deformities of florid osteomalacic rickets. Roentgen examination revealed evidence of numerous pathologic fractures. The liver was not enlarged.

In round numbers the following blood chemistry values were obtained: serum calcium 10 mg. per hundred cubic centimeters, serum inorganic phosphorus 2 mg., serum phosphatase activity 40 Bodansky units, total fixed base 156 milliequivalents per liter, carbon dioxide-combining power 35 volumes per cent and whole blood nonprotein nitrogen 30 mg. Normal values were obtained for sodium, chloride, osmotic pressure, protein, cholesterol and bilirubin. The urinary volume was somewhat increased, averaging 900 cc. daily in hot weather. The urine was consistently acid and invariably contained dextrose in concentrations varying from less than 1 per cent to 5 per cent: The daily excretion of dextrose amounted to approximately 25 Gm. Albuminuria, cylindruria and ketonuria were irregularly present. The daily excretion of organic acid, determined by the method of Van Slyke and Palmer, was greatly increased: The amount averaged ten times the normal values. A balance study revealed that the reserves of calcium and phosphorus were heavily taxed.

Unsuccessful efforts were made to influence the excretion of organic acid by altering the protein, carbohydrate and fat components of the diet. Qualitative chemical analysis demonstrated that approximately half of the urinary organic acids were amino acids; of the remainder, the largest portion was lactic acid; small amounts of other acids were detected. No improvement was procured with the usual therapeutic doses of vitamin D. Circumstances made it impossible to test the effect of alkali salts or of large doses of vitamin D.

The first case of this type of rickets was reported by Schier and Stern in 1926; the report of Fanconi in 1936 established its existence as a clinical entity. Including the present case, 3 examples have been recognized in this country. Accumulated anatomic evidence points to disturbance of hepatic function as the primary feature in pathogenesis; this appears to lead to faulty metabolism of protein, of carbohydrate or of both. Nephrotic degeneration of the kidneys is a usual, although not invariable, characteristic. This is tentatively interpreted as a phenomenon due to the excretion of normal chemical substances in pathologic amount. The frequency of consanguinity suggests that the disorders of metabolism are of genetic origin.

DISCUSSION

DR. EDWARDS A. PARK, Baltimore: An additional case of this condition is to be reported by Goldman and Ekstein in the *Journal of Pediatrics* (**15**:53, 1939). Each case seems to have its *spécialité,* and the case to which I refer has its *spécialité* in respect to treatment.

Dr. Guild attempted to correct the acidosis in her case through the administration of lactate and of sodium bicarbonate, but the condition of the patient became worse, and she was obliged to desist. The authors mentioned had the notion—the reasons were not entirely clear—that sodium would aggravate the condition but that potassium would alleviate it. They therefore fed the child a diet which was composed chiefly of potato, bananas and cocoa, and they reported that the negative phosphorus balance became positive and that the balances of sodium, chloride and potassium were much increased. The potassium and the phosphorus balance were affected more than the others.

Another peculiarity in their case was that the calcium was originally much elevated, being about 14 mg. per hundred cubic centimeters; under this treatment it rose to 17 mg. At the end of a month of treatment the glycosuria disappeared entirely.

The features mentioned were curious, namely, the complete reversal in the trend of the mineral metabolism accomplished by the change in diet and the high calcium values. One must have confirmation. But if the report is true, it is important.

I have been much interested in the question of what the mechanism producing rickets through acidosis actually is. I wish to ask Dr. McCune why acidosis produces rickets, and I shall be much pleased if he will bring to his assistance Dr. Darrow, Dr. Kramer, Dr. Hartmann and some of the chemists who are present.

DR. SAMUEL Z. LEVINE, New York: I do not represent the chemist. The matter that I want to present may appear superficially somewhat far afield from the discussion of the moment, but the notorious tendency of premature infants to have rickets is well recognized.

The usual conception that premature infants are susceptible to rickets because of their increased rate of growth is undoubtedly correct. However, an interesting recent finding is that a fair proportion of premature infants taking diets relatively high in protein excrete appreciable amounts of aromatic organic acids, presumably intermediary metabolites of tyrosine and phenylalanine.

If chemists come to the conclusion that acidosis predisposes to rickets, it will be interesting to speculate on the role which this transient organic acid acidosis may play in the patients' susceptibility.

DR. JULIAN D. BOYD, Iowa City: My co-workers and I have studied several patients with rickets associated with chronic acidosis. Dr. McCune mentioned 1 of these, a boy in whom rickets developed after ureteral transplantation. Whereas no relief was obtained from vitamin D and an adequate milk intake, the condition was controlled through the daily administration of sodium bicarbonate. We interpreted the condition as due to base deficit, induced through the withdrawal of fixed base in combination with the excreted acid radicals. Protracted acidosis will tend to draw out the calcium reserves, with attempted conservation of sodium. With correction of the base deficit or of the underlying acidosis, one expects restoration of normal mineralization of cartilage.

DR. ALEXIS F. HARTMANN, St. Louis: I agree with Dr. Boyd generally in his conception of the correlation of acidosis and rickets in various types of chronic renal insufficiency, but I am disturbed, as Dr. Park is, about the exact relationship. Certainly one can see acidosis without rickets, acidosis that lasts fairly long. Just recently my associates and I have observed a phenomenal infant.

For the first two months of life he got along well; then he began to present feeding difficulties. He would eat poorly, become listless and vomit. After two months of such symptoms he was brought in to us in a state of severe acidosis.

He was promptly relieved by parenteral administration of lactate, but about every five or six days thereafter the acidosis recurred to such a degree that treatment was again necessary.

The first time the carbon dioxide content was about 18 volumes per cent; it rose almost to 50 volumes per cent with the first parenteral injection of lactate. It slumped and was brought up again seven times in all, parenteral lactate therapy being necessary each time. In the meantime we tried to find out how much potential alkali must be given by mouth to prevent recurrence of acidosis. Finally, with the relatively huge amount of 75 cc. of a molar solution of sodium lactate daily, 15 cc. with each feeding, the acidosis was controlled.

Hastings' charts are excellently adapted to show acid-base balances and also the effect of sulfanilamide on these balances. The charts picture the four principal paths of displacement: carbon dioxide deficit alkalosis, acid excess or base deficit acidosis, carbon dioxide acidosis and alkali excess alkalosis.

Such a chart shows that this baby was in the position indicative of base deficit or acid excess acidosis.

Regardless of the carbon dioxide content of the blood, which might be under 30 volumes per cent, with the p_H distinctly low, the urine remained abnormally alkaline. The urine p_H always approximated the plasma p_H.

Apparently this baby had only one renal lesion. The tubules simply were unable to absorb barium carbonate. There was good output of phenolsulfonphthalein, and urea clearances were almost within normal limits.

At the age of about 5 months this baby had no evidence of rickets. Whether rickets will develop in time into the usual renal type, no one knows.

Dr. Daniel C. Darrow, New Haven, Conn.: I should like to point out several facts concerning the acidosis. Since the dissociation constant of amino acids is very small, amino acids can neither displace bicarbonate in the blood nor be combined with appreciable amounts of base at the p_H of the urine. On the other hand, lactic acid both displaces bicarbonate in the blood and will be excreted, either with fixed cations or with ammonia, in the urine. Hence if one could be sure that lactic acid was not formed from the urinary sugar after voiding, excretion of lactic acid could explain the acidosis in these patients.

However, it seems to me that the evidence of disturbed function of the tubules is more striking than the evidence of acidosis. First, Dr. McCune showed that the patients suffer from renal glycosuria, due to a disturbance in the reabsorption of dextrose from the glomerular filtrate by the tubules. The evidence seems equally convincing that the renal tubules fail to reabsorb enough phosphate from the glomerular filtrate to maintain the proper concentration of inorganic phosphorus in the serum. While it is possible for acidosis to cause increased excretion of phosphate, it seems unlikely that this is the case in these patients. Since the renal tubules fail to reabsorb dextrose normally, it is possible that the tubules also have a rather specific defect in the reabsorption of phosphate from the glomerular filtrate.

Dr. Benjamin Kramer, Brooklyn: In reporting the postmortem observations in her case yesterday morning, Dr. Guild failed to mention the changes in the bone. Knowledge of these changes is important. For years it has been believed, on the basis of roentgen evidence, that there is such a malady as renal rickets.

Now it is found that most patients with what has hitherto been designated as renal rickets are really suffering with chronic hyperparathyroidism. Furthermore, there are few authentic reports on the bones in the unusual forms of refractory rickets which have been discussed. For these reasons I should like to know just what the osseous changes were in Dr. Guild's case.

Dr. Edwards A. Park, Baltimore: In Dr. Guild's case the lesion in the bone was typical of deficiency rickets except that the destructive process seemed to be directed in a striking manner against the elements which contained lime salt. These elements seemed to be in process of preferential removal. I have never seen anything quite like it. One would find in some places, for example, that the whole lime salt interior of a trabecula was gone, leaving perhaps a U

of osteoid tissue. But except for the fact that the destructive processes in the bone were extremely marked, the lesion corresponded exactly to that of infantile rickets, showing no suggestion of hyperparathyroidism.

I should like to understand this matter myself. It is easy to say, Dr. Boyd, that acidosis produces rickets, but how does it do this? Rickets is a disease of the skeleton. If acidosis causes depletion of base, how does it produce rickets?

In rickets the newly formed bone is without lime salts. How does acidosis produce the lesion in the bone? At the first meeting of the Society of Experimental Biology and Medicine I ever attended, Dr. Henderson read a paper on shock. The evidence of shock consisted largely of the symptoms which patients on the operating table had shown. At the close of Dr. Henderson's paper, Dr. Meltzer rose and said, "I should like to ask one question, Dr. Henderson: What is shock?" Dr. Henderson struggled to his feet and recited some more illustrations. When he had finished, Dr. Meltzer rose again and said with great gravity, "I should like to ask Dr. Henderson one more question: What is shock?" Dr. Grulee, I should like to ask again: Why does acidosis produce rickets? Dr. Gyorgy has written a great deal on this subject.

DR. PAUL GYORGY, Cleveland: I have really nothing to add. I am glad that acidosis is again being considered in the pathogenesis of several forms of rickets.

In regard to Dr. Park's insistent query as to the manner in which acidosis produces rickets, of course I cannot explain it. I should like to add only one thought: Dr. Freudenberg and I have never believed that acidosis produces rickets merely by dissolving the calcium phosphate in the bone.

One of the consequences of acidosis is a disturbed calcium-phosphorus ratio in the blood. Furthermore, the acidosis produces a disturbance in cell metabolism. As the cells in the osteogenetic zone cannot work properly, the basis for rachitic disturbance is attributed to the same place. How and why these cells cannot function properly one cannot tell, but I do not know even one problem in diabetes concerning which one can really answer the question, What is diabetes? I am still optimistic, but I am disturbed that I cannot give a really proper reply, one which would mean that all the details of cell life are known. I think that no one, not even the youngest in this room, will answer the question.

DR. DONOVAN J. MCCUNE, New York: I have only two points to add. First, I agree with the ideas that Dr. Darrow has expressed. We have toyed in a dilettante manner with the idea that many of the changes are due to the inability of the tubules to reabsorb amino acids and phosphate, just as they are apparently unable to reabsorb sugar.

I chose to mention the acidosis because in the sense of this discussion it postulates a defect of tubular absorption.

GROWTH, DEVELOPMENT AND CARE OF THE CHILD. DR. HARRY BAKWIN and DR. RUTH MORRIS BAKWIN (by invitation), New York.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

PHYSICAL FITNESS IN THE CHILD AS REFLECTED BY CHANGES IN THE CARDIOVASCULAR SYSTEM AND IN BLOOD SERUM DURING EXERCISE. DR. FREDERIC W. SCHLUTZ, MINERVA MORSE, PH.D. (by invitation), and DR. JOHN L. GEDGOUD (by invitation), Chicago.

The problem represents an attempt to compare children as to nutritive state, physical capacity, cardiovascular changes and changes in blood serum during exercise.

The subjects were 12 children varying in age from 11 to 13 years. Four were Negroes. According to clinical estimate and Baldwin-Wood rating, 5 were undernourished, 3 obese and 4 normal.

For more accurate estimation of actual nutritive state, the children were measured by the anthropometric technic of McCloy, and their creatinine coefficients were determined. The results were expressed as indexes of weight, fat and muscle.

Appraising and interrelating these separate factors give a fairly accurate physical estimate of the actual structural makeup. On this basis 2 subjects had good musculature and 1, an obese boy, poor musculature. Two subjects were distinctly obese and 8 were underfat.

For rating physical capacity and changes in the cardiovascular system and in the blood serum during exercise, work was performed on a bicycle ergometer. Exercise was of two kinds: (1) moderate, with 55 revolutions of the pedal per minute, and (2) maximal, with 55 revolutions per minute for five minutes then as many revolutions as possible for one minute. The effort was recorded on a voltmeter.

Cardiovascular changes were determined by measuring pulse rate and systolic and diastolic pressure, with the child sitting in position on the bicycle, before exercise and approximately every fifteen seconds for two minutes after exercise.

Samples of blood for determination of changes in blood serum were taken from the opposite arm just after the blood pressure was read. Values of hemoglobin, cell volume, sugar p_H and total carbon dioxide were determined for whole citrated blood and values of lactic acid, phosphate, chloride, sodium and total nitrogen for serum.

With our somewhat limited material the correlation between physical capacity and nutritive rating was not clearcut. A larger series may show more consistent correlation. Age and cardiovascular factors apparently influence physical capacity.

Rise in pulse rate and pulse pressure with exercise bore no clearcut relation to physical capacity or nutritive state, but it was seemingly associated with both.

The most striking changes in the blood serum resulting from exercise were increases in lactate and decreases in bicarbonate. With moderate effort both bore a close relation to the physical capacity of the child. With maximal effort serum lactate increased still more, but the differences between individual children tended to disappear.

The extent of the lactate rise showed little relation to the nutritive state of the child, except that with maximal effort the 4 highest rises in lactate occurred in underweight children.

Other interesting changes in blood serum were small rises in serum phosphate which were negligible in children of superior capacity and marked in those of poorer capacity; a slight fall in blood sugar during moderate exercise for the children of superior capacity as compared with a slight rise in blood sugar for most of the other children, and a rise of serum protein which, with one exception, was marked for maximal work.

Because of the limited number of subjects these results, while they indicate certain trends, are more valuable as suggesting fruitful lines for further research.

DISCUSSION

DR. HAROLD L. HIGGINS, Boston: The use of maximal exertion as a measurement of physical fitness brings to mind certain observations which I made a number of years ago, when I was experimenting with alcohol. One of the experiments consisted in seeing how long a person could hold his breath. The breath could be held about a minute and a quarter under normal conditions; if the subject had previously taken a drink of alcohol the breath could be held for two and a quarter minutes. If the subject had been breathing oxygen, the breath could be held for two minutes, or less than after ingestion of alcohol; but with both oxygen and alcohol the breath was held three minutes. Therefore alcohol was distinctly a factor influencing the amount of maximum effort possible.

Similar work has been done in Leonard Hill's laboratory in London. The investigators had a subject raise his body as many times as possible on a timed schedule; they found that the maximum effort possible after alcohol was much

greater than it was under normal conditions. These observations refer to maximum effort over a short period, not to prolonged steady effort.

The explanation of these observations is that alcohol caused decreased appreciation of fatigue by the brain.

This principle explains why the most muscular person is not always able to show the greatest amount of maximum effort. Dr. Schlutz's data confirm this; that is, he has compared one child's brain with another's as to their inhibition of or reaction to fatigue. Has he a true measure of physical fitness?

Certain persons react more to fatigue than others; a given subject may react to fatigue more on one day than on another, for diet, infection (toxicity) or worry may vary the amount of maximum effort possible in a measured time.

GROWTH AND DEVELOPMENT OF NEWBORN INFANTS: FACTORS ASSOCIATED WITH OSSIFICATION OF CENTER FOR CUBOID BONE. DR. AMOS U. CHRISTIE, San Francisco, and DR. ETHEL C. DUNHAM and RACHEL M. JENSS, Sc.D. (by invitation), Washington, D. C.

In a study of the growth and development of 507 infants born alive in the wards of Johns Hopkins Hospital from May 1936 to June 1937, roentgenograms of the lower extremities made within seventy-two hours after birth and data in regard to maternal and fetal factors show the following association between the development of the center for the cuboid bone on the right and certain of these factors:

1. The race, sex and birth weight of the infant influence the development of the center of ossification for the cuboid bone. For example, it was found that this center was present more frequently in newborn Negro infants than in white infants; that within a given racial group it tended to be present more frequently in girls than in boys, and that for each race-sex group infants of higher birth weight tended to have the center present more frequently than infants of lower birth weight.

2. The development of the center is more advanced among infants whose mothers are multiparas and among infants born to older women.

3. The center is present more frequently in the more mature infants when birth length, birth weight or estimated period of gestation is used as a criterion of maturity.

It is hoped that this study of osseous development may be of practical value in making possible more exact estimates of fetal age and in relating skeletal maturity to physiologic and biochemical aspects of growth and development of newborn infants.

DISCUSSION

DR. HAROLD C. STUART, Boston: Some figures concerning a series studied by my associates and me do not quite agree with Dr. Christie's data in respect to relation to weight. In our series, as recently reviewed, there were 235 children, about equally divided between boys and girls, all white and relatively homogeneous from the racial standpoint. We excluded from the series all babies of birth weight under 5 pounds (2,268 Gm.), so that infants who were definitely born prematurely are not included; within the group the birth weight ranged from 5 to 10 pounds (4,536 Gm.). An attempt was made to correlate osseous development with sex, with weight and length at birth and with date of expected confinement.

The osseous rating used was based on consideration not of the cuboid bone alone but of all the centers. The sex difference frequently referred to was clearly shown in our series. There was practically no correlation between osseous rating and birth weight or expected date of confinement. The correlation between osseous development and birth length was considerably better, being 0.39 for boys and 0.48 for girls.

The point is that although all of the factors to which Dr. Christie has referred are probably operative in determining the stage to which osseous development has

progressed at the time of birth, there is still a wide range between individuals, not only at birth but at later ages, which is not explained by these considerations.

DR. ARTHUR H. PARMELEE, Oak Park, Ill.: Dr. Christie's paper brings out the difficulties one has in determining the actual state of maturity of the infant at the moment of its birth. This state is influenced by a variety of factors. Physicians have long since discontinued reliance on the obstetric idea that prematurity may be determined by computation of the supposed length of gestation.

Now one can see that skeletal growth also is dependent on many factors, and those who have examined a great many roentgenograms of long bones and have attempted to evaluate skeletal maturity by the condition of ossification of the epiphysial centers at birth find here also an enormous variation. For example, the idea that the presence of the center in the lower epiphysis of the femur is an important indication of the maturity of the newborn infant is undependable. I have seen that the center was present in definitely premature infants and have noted its absence in full term infants. I believe that somatic, especially skeletal, development is probably dependent on many more factors than physiologic development. Some of the physiologic processes, for example, the so-called pregnancy reactions, which depend on the presence in the infant of certain estrogenic substances, will prove more dependable in evaluating maturity than the signs of somatic growth. These reactions depend on the passive transfer of estrogenic hormones which are at their peak of concentration in the mother's blood in the very last week of pregnancy.

The presence or absence of such pregnancy reactions as engorgement of the breast and lactation I have learned to depend on greatly as an indicator of maturity. Engorgement of the breast and lactation are never found in premature infants, while they are very rarely absent from infants obviously born at full term.

I believe that evidences of physiologic maturity are more dependable than skeletal growth for estimating the state of maturity of the infant at birth.

DR. HARRY BAKWIN, New York: Variation in ossification at the wrist is wide. Of white girls, about 20 per cent show one or more ossification centers at birth; yet it is not until about the age of 9 months that 100 per cent of white girls show ossification of a center at the wrist. Boys show a similarly wide variation. About 10 per cent of newborn boys show an ossification center at the wrist, but it is not until about the age of 1 year that all white boys reach this stage.

This great variability persists throughout the period of growth. Some normal children at 1 year show as advanced a stage of ossification as do other normal children of the same sex and race at 5 years. This is important from a practical standpoint. It is dangerous to diagnose developmental retardation on the basis of the stage of carpal ossification without due regard to the clinical condition of the child.

Carpal ossification is an index of maturity only in a limited sense. Maturity means the completion of the developmental process. There is no evidence to indicate that the rate of carpal ossification is related to other aspects of development.

DR. ALFRED H. WASHBURN, Denver: In recent years I have been a proponent of individual variation. I think that perhaps there is danger of overdoing this attitude, and I am tempted to qualify my concept of individual variation.

There is of course, as Dr. Bakwin has said, a tremendous amount of individual variation in the time of appearance of the various epiphysial centers. That fact should remind one that in spite of great individual variation, the situation is not at all chaotic, that for any given individual there is an orderly pattern of maturation. The work presented by Dr. Christie is highly serviceable in showing that it is possible to sort out the factors that are responsible for making the pattern of a given individual different from that of another individual.

DR. ETHEL COLLINS DUNHAM, Washington, D. C.: Dr. Christie's paper represents a groping toward some method of determining the maturity of the infant. In such attempts it is apparent that one labors under many difficulties.

For example, in a study of the weights of a large number of infants born consecutively it is found that a large number of infants weigh between 3,000 and 4,000 Gm. but only a small number weigh less than 1,500 or more than 4,000 Gm. The latter group in particular should be studied with regard to maturity as compared with the group of intermediate weight.

Also, one is hindered in studying maturity by the incompleteness of the information available with regard to the mother's pregnancy. One should know the influence of various complications of the mother's pregnancy on the development of the infant, but it is almost impossible to find out exactly when a complication started, how severe it was and when it ended. Obviously, unless such information is exact the effect of the various complications on the growth and development of the infant cannot be determined.

Another handicap lies in preconceived ideas of prematurity. I cannot help reiterating what I say on every occasion that offers: that there is no satisfactory definition of a premature infant except the child is born more than two weeks before the end of nine months of pregnancy. As is well known, such an infant needs special care. Even if, so far as is known, the infant is not born prematurely, low birth weight should be regarded as one criterion for the need of special care.

As pediatricians we are chiefly interested in discovering better criteria for selecting the infants that need special care, in an effort to improve their chances of survival.

DR. CHARLES G. KERLEY, New York: The question resolves itself largely into a consideration of osseous development of retarded children and its relation to somatic development.

Every child who comes to me showing retarded growth, mental or physical, has the benefit of roentgen study of the wrist, knee and ankle. This is of so much service that I should be working under a heavy handicap where it denied me.

ROENTGEN STUDIES OF PATTERNS OF GROWTH OF MUSCLE AND OTHER TISSUES IN YOUNG CHILDREN. DR. HAROLD C. STUART, Boston.

The primary purpose of this study was to throw light on the growth of skeletal muscles. This was part of a broader undertaking to recognize and evaluate the differences in build, posture and physical adequacy encountered among children. The method adopted also afforded an opportunity to measure the amount of bone, skin and fat which, together with muscle, compose the segment of skeletal mass under study. The investigations being reported at this time deal first with a technic for estimating the relative amounts of these tissues in a given area of the right leg by measuring the shadows which they cast on roentgenograms taken under standard conditions. The report presents norms for the various measurements obtained for successive ages from 3 months to 6 years and shows the distributions for the different variables for boys and girls at 5 years. Second, growth curves for the variables studied are presented for selected children from a normal group,[1] and data are also given for a few abnormal children.

The roentgenograms used in this study are anteroposterior views of the leg area, taken at 3 foot (90 cm.) tube distance and with such exposure as will clearly differentiate the three types of shadows. The area studied is that bounded by parallel lines tangent to the ends of the tibial shaft. The weights and the equivalent areas of the shadows of bone, muscle, skin and fat and the total area are obtained, as well as the measures of certain breadths and the length of the shaft of the tibia. Numerous observations as to the reliability of the technic described have been made. These studies indicate that the method of weighing roentgen

1. The composition of this group and the studies being made upon them are fully described in Stuart, H. C., and others: Studies from the Center for Research in Child Health and Development, School of Public Health, Harvard University, I. The Center, the Group Under Obseravtion, Sources of Information, and Studies in Progress, Monograph of the Society for Research in Child Development, National Research Council 1939, vol. 4, no. 1 (serial no. 20).

shadows has value both for clinical purposes and in research. The amounts of muscle shadow, as determined for a group of cases, are compared with the creatinine excretions in the urine of these children.

There is a pattern of growth in the mass of bone, muscle, skin and fat. This is shown both in curves representing the averages of the amounts of tissue shadows and in curves plotting the average percentage distribution between the tissues at succeeding ages. As would be anticipated, the amount of each shadow is in part a function of age and in part of tibial length. Furthermore, the extent of the individual differences in the amounts of these tissues is great among children of the same age or with tibias of the same length. The method apparently gives measurable evidence as to the fundamental differences in build, body type and fat storage between different children and in the same child at different ages. Sex differences have not been determined except for 5 year old children. At this age there appears to be no consistent difference in amount of bone or muscle, but girls show a considerably greater amount of skin and fat.

It is proposed to correlate the material obtained by this method with data obtained by the usual methods of examination of the children under study at the Center for Research in Child Health and Development at Harvard University and to present the findings in a subsequent report. Data presented at this time, however, show that the children in this normal series belong to widely different types in respect to the amounts of these tissues. They also show that irregular or abnormal growth may be demonstrated and its degree measured by this method.

The importance of recognizing the fractions of the total body mass represented by the different tissues is emphasized, and the usefulness for this purpose of a roentgenogram, studied in a simple standard way, is suggested.

DISCUSSION

Dr. Frederic W. Schlutz, Chicago: Dr. Stuart used the term "obese underweight." That is not really a contradiction. One of the children I observed could be so described. He proved to be the child in the series who was most inadequate as to physical capacity, and showed the most pronounced changes in acid base rate and cardiovascular adjustment.

Dr. Ethel Collins Dunham, Washington, D. C.: In Dr. Stuart's work much depends on the weight of the cut sections of films. First, have any tests of accuracy been made in connection with the cutting? In my experience the outline of the soft tissues in roentgenograms is not clear, and this would make accurate cutting difficult. Second, is there any evidence that all roentgen films weigh the same? Even if films made by one firm of manufacturers were used throughout the experiments, would they be uniform in weight?

Dr. Fritz B. Talbot, Boston: Has Dr. Stuart made any attempts to correlate his roentgen findings with the postmortem measurements and weights?

Of course, this method of attack is important because it proves to be an accurate measurement (I am not sure whether Dr. Stuart used the word "measurement") it certainly is an estimate of the relative amount of fat, muscle and protein in the body, and such estimates are essential for all fundamental problems of physiology.

I believe that in most instances in which wrong conclusions have been reached the lack of the data which Dr. Stuart is trying to supply is responsible. I think that even if he has not found the final answer, his approach may develop into one of the highly important contributions to the knowledge of physiology.

Dr. Lawson Wilkins, Baltimore: Is there any correlation of the measurement of this particular segment of the body with that of the body as a whole? All physicians are familiar with people who have fat legs but are not necessarily large all over.

Dr. Alfred H. Washburn, Denver: I am particularly interested in Dr. Stuart's work because it brings up a point that is frequently neglected: the usefulness of roentgenograms as a means of measuring perfectly ordinary anatomic

structure in the developing child. For instance, one obtains a much more accurate measurement of growth, with a curve that will not jiggle up and down nearly so often, if one measures the length of a given long bone from year to year than if one accepts the anthropometrist's measures. There are many similar illustrations of the useful information furnished by roentgen study.

Has Dr. Stuart applied this technic to any other part of the body besides the leg?

DR. HAROLD C. STUART, Boston: My associates and I have conducted a number of studies on the reliability of our technic. I do not wish to give the impression that we believe we have an absolutely accurate method for measuring the amount of these tissues; we know that we have not. We were surprised, however, to find how closely our measurements agreed when we repeated the observations on the same child at the same examination. We have tried changing the position of the tube with the child's position kept as constant as possible, and we have also tried the effects of various changes in the child's position with the tube and other technical factors kept constant. External or internal rotation of the leg and flexions of the knee, if they are present in more than moderate degree, cause an appreciable difference in the values obtained. Whether the muscles are contracted or relaxed seems to make little difference. However, a number of precautions must be taken in securing the roentgenograms if comparable results are to be obtained. When two roentgenograms are taken at the same time in the same cassette, the differences in measurements and values obtained by different people which are due to differences in outlining, cutting up and weighing the segments of film are negligible. The details of these tests of reliability and objectivity will be given in subsequent published reports of these studies.

As to the possible differences in the weight of the unit areas of different films, we have not tried different makes of films. We have weighed given areas of different films, and it was in this connection that I made reference to the accuracy of Miss Hill's technic. She outlines the shadows between the tissues with pen on an illuminator and cuts along these pen lines in reflected light. The greatest possibility of error with this technic lies in the attempt to outline shadows which are poorly differentiated because of poor exposure. Films so exposed should be discarded. The charts on the whole reveal surprisingly satisfactory consistency in the curves produced by plotting repeated measurements, although an occasional measurement is obviously in error.

I omitted two or three slides which I had hoped to include in presenting this report. One of these showed the measurements obtained by Weinbach for the actual volume of tissues in the case of ours which he studied. The curves produced by his estimates of volume and our estimates of area were satisfactorily similar.

We have not as yet tried to obtain actual values for the weights of the respective tissues from amputated or postmortem material of which roentgenograms had previously been obtained.

I may have used the word "measurements" of skin, fat and muscle inadvertently. We intended to use the word "estimate" or the expression "relative measurement," because these measurements pertain only to shadows and bear merely an indirect relation to the actual quantities of tissues.

As to the differences between the amounts of tissues in different parts of the body, these obviously exist, and our technic as thus far applied takes no account of them. Weinbach has studied the amounts of the tissues in the forearm by his method, and this should be possible with our technic also. We have attempted to describe, on the basis of clinical examination, the proportions and development in arms and other parts, for instance, to ascertain whether there is a fat girdle. We have then tried to take these factors into account in studying individuals and in interpreting our roentgen data.

(To be concluded)

Book Reviews

Economical Administration of Health Insurance Benefits: Part I. The Principle of Economy in the Administration of Health Benefits. By Dr. Walter Pryll. No price given. Pp. 137, with no illustrations. Geneva: International Labour Office, 1938.

Dr. Pryll goes extensively into the economical administration of health insurance benefits for recipients of medical care under a health insurance plan. A brief abstract of this article is hardly possible because of the many instances in which the medical care required may be both extensive and varied. Under the general title of health benefits, the author enumerates extensively the need of giving attention, first of all, to the diagnosis of the illness of the particular patient. He emphasizes with frequent repetition the absolute need of taking cognizance of all the various factors, physiologic, psychologic, and biologic, that enter into the correct diagnosis of the illness of any person. It is essential to arrive at a correct diagnosis before therapy in any of its varied forms can be intelligently instituted. Therapeutic measures are discussed with equal broadness in their possible and practical application to each patient who is to be the recipient of medical care under the proposed plan. No specific outline of the source of funds to carry out such a system of health insurance benefits is presented. When the question of costs of medical care under this general plan is considered, emphasis is placed on the almost absolute necessity of economy if the plan is to survive. The conclusion seems almost inevitable that Dr. Pryll has been carried away by wishful thinking instead of proving conclusively that these two elements, complete medical care in its fullest sense and reasonably adequate compensation for the members of the medical profession who are to administer this service, can be practically harmonized. Dr. Pryll indicates many factors that will make the successful administration of this or of similar systems difficult, if at all practicable. This presentation of the subject merits careful study. I believe it warrants the conclusion that while the results that are hoped for are desirable, medically, efficient care and financial economy as advocated are incompatible. More emphasis is laid on the need of economy in administering the funds of health insurance benefit plans than on reasonable and adequate compensation for the members of the medical profession, without which any such plan is an impossibility. Wishful thinking and optimism without foundation characterize the presentation of this thesis.

The Patient as a Person. By G. Canby Robinson, M.D. Price, $3. Pp. 423, with no illustrations. New York: Commonwealth Fund, Division of Publications, 1939.

This book primarily attempts to emphasize the relation of the mind to the body and to force recognition of the difference between illness and disease. A person suffering from a definite somatic disease may not feel ill, and the cause of many an illness may rest entirely in the fields of conscious and subconscious thought, with resulting disturbances in bodily function but no discoverable somatic disease. In addition, instances are being found of disturbances of bodily functions which lead in time to somatic changes. By the method of presenting case histories Dr. Robinson discloses the sociologic background of various routine types of hospital patients and proves conclusively that failure to take this factor into account may completely prevent cure of the illness from which the patient is suffering. He makes a plea for the formal attempt to teach medical students this psychobiologic concept of the patient. Furthermore, he points out the obvious facts that most sociologic dislocations involve the family as a whole and that therefore the general practitioner is in a much better position to evaluate and, if possible, to alleviate them than is the specialist, whose concern is primarily with one member of the family. For all practitioners and especially for those who are beginning practice this book cannot fail to be informative and stimulating.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 3-5, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Prof. Charles McNeil, 44 Heriot Row, Edinburgh, Scotland.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: Nov. 16-18, 1939.
Region I. Place: Mayflower Hotel, Washington, D. C. Time: April 4-6, 1940.
Region IV. Place: Seattle, Wash. Time: May 30-June 1, 1940.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Daniel C. Darrow, 330 Cedar St., New Haven, Conn.
Secretary: Dr.Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.
Place: Memphis, Tenn. Time: Nov. 21-24, 1939.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Secretary: Dr. George N. Leonard, 605 Lincoln Rd., Miami Beach.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. L. H. Muse, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Scientific Meeting: Place: Atlanta. Time: December 1939. Business Meeting: Place: Savannah. Time: April 1940.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Phillip C. De Verges, Audubon Bldg., New Orleans.
Secretary-Treasurer: Dr. W. C. Rivenbark, 220 Physicians and Surgeons Bldg., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.
Secretary-Treasurer: Dr. William Weston Jr., 1428 Lady St., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: T. A. Tumbleson, 2100 North St., Beaumont.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Fort Worth. Time: Oct. 14, 1939.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Samuel T. Levethan, 254 E. 184th St., Grand Concourse, New York.
Secretary: Dr. David Greene, 910 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. Harold Nesbit, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140–2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St. N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. James H. Park Jr., 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Thomas J. Donovan, 2418 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn, N. Y.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry H. Donnally, 1612 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of October, January, February, March and April.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Secretary-Treasurer: Dr. Samuel E. Kohn, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. R. E. Nutting, 205 W. 2d St., Duluth, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Samuel Goldberg, 4546 N. Broad St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., first Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of each month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. E. Earl Moody, 829 S. Alvarado Ave., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Clement Smith, 1101 Beacon St., Brookline, Mass.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.